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**Migraine Beyond Pain: An Investigation into the Non-Painful
Characteristics of Migraine as a Cyclical Disorder**

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Here was something which could pass, in a few minutes, from the subtlest disorders of perception, speech, emotion and thought, to every conceivable vegetative symptom. Every patient with classical migraine opened out, as it were, into an entire encyclopaedia of neurology.

Oliver Sacks, *Migraine*.

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Abstract

This thesis aims to investigate the complex symptomology of migraine as a cyclic neurological disorder. The literature on migraine is primarily focused on the pathophysiological underpinnings of the migraine headache and pharmacological interventions. However, some migraine research has highlighted that the migraine headache merely constitutes a singular phase of the condition that is preceded by the migraine prodrome and followed by the migraine postdrome. Rather than being characterised by pain, the prodrome and postdrome phases are distinguished by changes in behavioural, affective, and cognitive states. This is the first theoretical framework of this thesis. The second framework used in this thesis is the circadian framework, which examines the daily rhythmic fluctuations in physiology and behaviour. These two frameworks, although distinct, have considerable anatomical and symptomatic overlap with both implicating sleep, eating behaviours, activity, and thermoregulation. As such, the impact of migraine goes beyond the severity of pain and reflects comprehensive disability. This thesis examines circadian behaviours and psychological factors in individuals with migraine compared to non-migraine individuals, within migraine frequency groups and across the phases of migraine.

To establish the level of cognitive impairment in individuals with migraine, Chapter Two of this thesis reviews the current literature on neuropsychological functioning in adult migraineurs published over the last two decades. Chapter Three investigates cross-sectional associations of sleep and eating factors in migraine and examines the differences in sleep and eating behaviours between individuals with and without migraine. Chapter Four subjectively examines migraine using semi-

structured interviews and highlights the dimensional lived experience of migraine that impairs the individual physically, psychologically and socially. Chapter Five investigates the longitudinal associations of sleep (subjective and objective), self-reported mood, stress, and fatigue, self-reported changes in perceived temperature and appetite, activity (step count) and heart rate variables in affecting migraine onset, characteristics, and phases. This chapter further investigates associations of neuropsychological functioning and phase structured by testing session. Chapter Six examines participants' experiences participating in the longitudinal study outlined in Chapter Five to enable insight and adaptation for future research using similar designs.

The findings of this thesis highlight the need for migraine to be recognised as a cyclic disorder that has physical, behavioural, psychological, and social implications in both research and practice but also at a population level where it is frequently misunderstood. The findings warrant further investigation into the role of circadian rhythms in migraine pathophysiology and the overlap in migraine symptoms and circadian behaviours. Future research is needed to clearly establish the psychological, behavioural, and temporal characteristics of each of the migraine phases.

Abbreviations

5-HIAA	Urinary 5-Hydroxyindoleacetic Acid
5-HT	Serotonin
AD8	Ascertain Dementia 8 Questionnaire
AEBQ	Adult Eating Behaviour Questionnaire
AES-S	Self-version of Apathy Evaluation Scale
ANT	Attention Networks Test
APA	American Psychiatric Association
BDI	Becks Depression Inventory
BDI-SF	Becks Depression Inventory Short Form
BFRT	Benton Face Recognition Test
BMAL1	Brain and Muscle Aryl Hydrocarbon Receptor Nuclear Translocator like 1
BML	Backward Maximum Length
BMS	Backward Memory Span
bTETT	Backward Two-Error Total Trials
CBF	Cerebral Blood Flow
CBP	Chronic Back Pain
CBT	Cognitive Behavioural Therapy
CERAD-WLMT	Consortium to Establish a Registry for Alzheimer's Disease Word List Memory Test
CGRP	Calcitonin Gene Related Peptide
CI	Confidence Interval
CM	Chronic Migraine
CMwMOH	Chronic Migraine with Medication Overuse Headache
CNS	Central Nervous System
cRBF	Cerebral Regional Blood Flow
CrI	Credible Intervals
CRY	Cryptochrome
CSD	Cortical Spreading Depolarisation
CVLT	California Verbal Learning Test
DBT	Dialectical Behaviour Therapy

DDT	Dichotic Digit Test
D-KEFS	Delis-Kaplan Executive Functions System Colour-Word Interference Test
DNA	Deoxyribonucleic Acid
DPT	Duration Pattern Test
DSST	Digit Symbol Substitution Test
EEG	Electroencephalography
EOG	Electrooculogram
EM	Episodic Migraine
ENB-2	The Brief Neuropsychological Examination
FHM	Familial Hemiplegic Migraine
GDS	Geriatric Depression Scale
GIN	Gaps in Noise Test
GNG	Go, No-Go Test
GRE	Greyscale Task
HADS	Hospital Anxiety and Depression Scale
HC	Healthy Controls
HDI	Healthy Diet Index
HPD	Highest Posterior Density
ICHD	International Classification of Headache Disorders
IGT	Iowa Gambling Task
IHS	International Headache Society
ipRGC	Intrinsically Photosensitive Retinal Ganglion Cells
ISI	Insomnia Severity Index
KSQ	Karolinska Sleep Questionnaire
LC	Locus Coeruleus
LM	Landmark Task
LOT	Line Orientation Test
M1	Primary Motor Cortex
M2	Secondary Motor Cortex
MAET	Motion After Effect Task
MCTQ	Munich Chronotype Questionnaire
MDD	Major Depression Disorder

MDDT	Motion Direction Discrimination Task
MERTK	C-Mer Proto-Oncogene Tyrosine Kinase
MIDAS	Migraine Disability Assessment
MIST	Memory for Intentions Screening Test
MMSE	Mini Mental State Examination
MoCA	Montreal Cognitive Assessment
MOH	Medication Overuse Headache
MSF	Midsleep on free days
MSFsc	Midsleep on free days sleep corrected
MwA	Migraine with Aura
MwoA	Migraine without Aura
NMH	Non-Migraine Headache
NREM	Non-Rapid Eye Movement
OFC	Orbitofrontal Cortex
OR	Odds Ratio
OSA	Obstructive Sleep Apnoea
P	Probability Value
PACAP	Pituitary Adenylate Cyclase-Activating Peptide
PAG	Periaqueductal Gray Area
PDQ	Perceived Deficits Questionnaire
PER	Period
PPTH	Persistent Post-Trauma Headache
PSG	Polysomnography
PSQI	Pittsburgh Sleep Quality Index
RAET	Rutgers Acquired Equivalence Task
RAVLT	Ray Auditory Verbal Learning Test
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
REM	Rapid Eye Movement
REML	Rapid Eye Movement Latency
RMSSD	Root Mean Square of Successive Differences
ROCF	Rey-Osterrieth Complex Figure Test
RVM	Rostral Ventral Medulla

S	Somatosensory Cortices
SATB2	SATB Homeobox 2
SCN	Suprachiasmatic Nucleus
SD	Standard Deviation
SE	Standard Error
SFT	Semantic Fluency Test
SJL	Social jetlag
SMQ	Subjective Memory Complaints Questionnaire
SOL	Sleep Onset Latency
SPG	Sphenopalatine Ganglion
SREBQ	Self-Regulation of Eating Behaviours Questionnaire
STN	Spinal Trigeminal Nucleus
STT	Shape Trail Test
SuS	Superior Salivatory Nucleus
TCC	Trigemino-cervical Complex
TG	Trigeminal Ganglion
TMT	Trail Making Tests
TMTA	Trail Making Test A
TMTB	Trail Making Test B
TRT	Total Record Time
TST	Total Sleep Time
UFL1	Ubiquitin Fold Modifier 1
V	Visual Cortices
VIP	Vasoactive Intestinal Peptide
VTAPBP	Ventral Tegmental Parabrachial Pigmented Nucleus
WAIS-III	Wechsler Adult Intelligence Scale Third Version
WASI	Wechsler Abbreviated Scale of Intelligence
WASO	Wake After Sleep Onset
WMS-III	Wechsler Memory Scale Third Version

Chapter One

Literary Review

1.1 Introduction

This chapter will provide an overview of the migraine literature to provide a basis for understanding the theoretical underpinnings for the empirical chapters of this thesis.

As the understanding of migraine has changed over time, with various theories on the mechanisms of migraine, this chapter will try to provide a chronological understanding of migraine as it has developed in the literature. The chapter will look at the diagnostic criteria for migraine, the epidemiology of migraine, the pathophysiological underpinning of the migraine headache and prodrome and postdrome phases. This chapter will then introduce the literature on circadian rhythms and sleep and move on to examine the literature on circadian rhythms in migraine and the overlap in circadian and migraine systems through behaviours such as sleep and eating. The psychosocial impact of migraine will then be explored, looking at the impact of migraine beyond pain to include effects on cognition and day-to-day functioning in society. Finally, the chapter will discuss the current pharmacological, psychological and behavioural approaches to migraine treatment. Following this, the rationale for the empirical chapters will be outlined with reference to two key theoretical frameworks including the circadian framework and the cyclical nature of migraine (Karsan & Goadsby, 2018; Roenneberg et al., 2019; Takahashi et al., 2018). The chapter will conclude with an overview and rationale for the chapters to follow.

1.2 Migraine

1.2.1. History of migraine and diagnostic criteria

Although migraine has been recognised as a distinct condition for centuries, descriptions of symptoms resembling migraine can be traced to antiquity. The

earliest records of ritualistic treatment of migraine are traced back to ancient civilisations of Mesopotamia, circa 4000 B.C. (Magiorkinis et al., 2009). Later Sumerian incantations against headache are preserved in Neo-Assyrian and Late Babylonian medical texts dating to the first millennium B.C.E (Bácskay, 2019). Descriptions of visual disturbances preceding severe unilateral headache have further been documented in the medical writings of Hippocrates circa. 460-377 B.C.E, an account of a condition consistent with migraine with visual aura (Weatherall, 2021). Approximately two centuries later, Aretaeus described the condition he termed heterocrania (circa 130-180 B.C.E.).

For they flee the light; the darkness soothes their disease: nor can they bear readily to look upon or hear anything agreeable; their sense of smell is vitiated, neither does anything agreeable to smell delight them, and they have also an aversion to fetid things: the patients, moreover, are weary of life, and wish to die (Adams, 1856).

The term ‘Hemicrania’, derived from the Greek ‘hemi,’ half, ‘crania,’ skull, referred to the defining presentation of migraine as pain on one side of the head. While this is the most distinguishable symptom of the disorder, in recent years migraine has come to be recognised as a complex disorder of the nervous system (Karsan & Goadsby, 2017).

To be diagnosed with migraine, one must meet the criteria outlined by the *International Classification of Headache Disorders* (2018). The duration of the pain in migraine lasts at least 4 to 72 hours. The migraine attack must meet two of the following conditions: unilateral location of pain, moderate to severe pain intensity, pulsating quality or pain that is aggravated by physical activity (Headache

Classification Committee of the International Headache Society [IHS] 2018).

Migraine without aura is the most frequent migraine diagnosis observed across the condition. The attack must also coincide with experiences of at least one of the following: nausea, photophobia or phonophobia (IHS, 2018). If the individual experiences aura prior to the onset of pain, they will be diagnosed with migraine with aura. However, if there are attacks in which aura does not occur, a secondary diagnosis of migraine without aura is also received (IHS, 2018). Aura typically presents visually, sensory and language impairments however may appear as reversible motor, retinal or brainstem dysfunction for up to one hour prior to the onset of migraine pain (IHS, 2018). If visual aura presents a unilateral location the diagnosis of retinal migraine may be given following a visual field examination and patients' description of the visual field defect. This may present as scintillation, scotoma, or blindness (IHS, 2018).

Some patients may further experience brainstem aura which entails two reversible symptoms of dysarthria (slow or slurred speech), vertigo, tinnitus, hyperacusis (sensitivity to noise), diplopia (double vision), ataxia, or reduced consciousness (IHS, 2018). The presence of motor weakness or paralysis is the diagnostic marker of hemiplegic migraine. Hemiplegic migraine is migraine with aura which includes motor weakness (IHS, 2018). Motor weakness in this condition however can be much longer than that which is present in typical migraine with aura and may last several weeks although the average duration would be under three days (IHS, 2018). If a family member further displays the same symptoms of migraine with aura including motor weakness, a diagnosis of familial hemiplegic migraine is given. This form of migraine has been found to have a significant genetic component with specific gene mutations associated with several types of FHM (IHS, 2018).

Migraine with or without aura, which exceeds 15 or more days a month, qualifies the diagnosis of chronic migraine. This diagnosis is isolated from the others as it is impossible to distinguish the number of attacks as they occur so frequently (IHS, 2018). Medication overuse headache must further be disqualified as reduction in medication use may reduce the frequency of headache days in those who are not actually chronic (IHS, 2018). If the migraine pain of a single attack persists for more than 72 hours the patient is diagnosed with status migrainosus (IHS 2018). Migraine can be further accompanied by coexisting episodic syndromes. Such syndromes include recurrent gastrointestinal disturbance, cyclic vomiting syndrome, abdominal migraine, or migraine related vestibulopathy; vestibular migraine. Further complications of migraine include persistent aura, migrainous infarction and migraine aura-triggered seizure (IHS, 2018). Finally, it must be evaluated if the presence of migraine may better be explained by the onset of an aggravating or secondary condition. The presence of a secondary condition or event such as, but not limited to, head trauma, substance abuse, withdrawal and infection among others, may explain the onset of migraine as a symptom of another condition, a secondary migraine rather than primary migraine (IHS, 2018).

Table 1.1. Table outlining the International Classification of Headache Disorders (3rd edition) diagnostic criteria for migraine without aura and migraine with aura.

Symptoms must not be better accounted for by another ICHD-3 diagnosis.

<i>Diagnosis</i>	<i>Reversible aura symptoms</i>	<i>Aura Characteristics</i>	<i>Pain Duration</i>	<i>Pain Characteristics</i>	<i>Associated Symptoms</i>
<i>Migraine without aura</i>	None	None	4-72 hours (untreated)	At least two of the following: unilateral location, pulsating quality, moderate to severe pain, aggravation by or causing avoidance of routine physical activity	At least one of the following: Nausea, photophobia and phonophobia
<i>Migraine with aura (aura with headache)</i>	One or more of the following: visual, sensory, speech and/or language, motor, brainstem, retinal	At least three of the following: at least on aura symptom spreads gradually over ≥ 5 minutes, Each aura symptom lasts 5-60 minutes, at least aura symptom is unilateral, at least one aura symptom is positive (scintillations, pins and needles), the aura is accompanied or followed within 60 minutes by headache	4-72 hours (untreated)	At least two of the following: unilateral location, pulsating quality, moderate to severe pain, aggravation by or causing avoidance of routine physical activity <i>Some headaches following aura, however, may not meet these criteria and are still considered migraine headache</i>	Nausea, photophobia and phonophobia

1.2.2. The Prodrome

The 24-48 hours prior to the onset of migraine pain is considered the prodrome phase of migraine. This phase is also prior to the experience of aura. During this time, migraineurs commonly report symptoms such as yawning, mood changes, appetite changes, tiredness, thirst, neck stiffness, and changes in cognitive function (Karsan & Goadsby, 2018). Of these symptoms, many implicate the hypothalamus. A narrative review by Karsan and Goadsby (2023), synthesised the literature on neuroimaging studies during the premonitory phase. In this review, studies using resting state functional magnetic resonance imaging, arterial spin labelling perfusion, diffusion tensor imaging, and positron emission tomography during induced and spontaneous migraine attacks were examined (Karsan & Goadsby, 2023). The studies included in the review found impaired and disordered brain functioning in the hypothalamus, basal ganglia, midbrain, pons, spinal trigeminal nuclei, and limbic system (Karsan & Goadsby, 2023). Such brain areas are involved in pain, sensory, limbic and regulation or in this case, dysregulation in migraine pathology (Karsan & Goadsby, 2023). During a nitro-glycerine induced attack, Maniyar et al. (2014) observed increased cerebral blood flow in the nucleus tractus solitarius of the medulla in migraineurs experiencing nausea in comparison to those with no nausea, suggesting this area to be functionally associated with nausea in the prodromal stage of migraine.

In another study, Maniyar et al. (2014) observed increased early prodromal activation of various brain areas including the right posterior hypothalamic region, right substantia nigra, right periaqueductal grey, right dorsal pons, right and left putamen, right caudate nucleus. Similarly increased activation was observed in the right and left occipital cortex and cerebellum, right prefrontal cortex, right frontal

cortex, right temporal cortex, right anterior and posterior cingular, right pulvinar nucleus of thalamus and the left parietal cortex (Maniyar et al. 2014b). However, by the onset of migraine pain in the headache phase, increased activation is localised to the dorsal pons, insula, frontal and parietal cortex and the cerebellum (Maniyar et al. 2014b). Maniyar et al. (2014b) suggest that such activations may explain many premonitory symptoms such as yawning, frequent urination, thirst related to dopaminergic mechanisms of the hypothalamus and substantia nigra.

Similarly, connections between the hypothalamus and the limbic system may be involved in mood changes observed in this phase. Neurotransmitters related to the hypothalamus such as the dopamine and orexin A and B have further been implicated in symptoms such as feeding, sleep, arousal, and autonomic functioning (Maniyar et al. 2014b). Further supporting the role of hypothalamic involvement in the prodrome is a study by Schulte and May (2016) who have observed altered connectivity between the hypothalamus and the spinal trigeminal nucleus and dorsal rostral pons, amygdala, and hippocampus (Schulte et al., 2018). Further imaging studies such as that by Stankewitz et al., (2011) observed increased activity in the spinal trigeminal nucleus during the prodrome compared to during the headache phase and following, between attacks. Further research by Meylakh et al. (2018) also demonstrated increased activity in the hypothalamus, brainstem, trigeminal nucleus, and dorsal pons during the prodrome compared to the headache phase, postdrome and between attacks.

The prodrome and its relative premonitory symptoms are like that which is reported by patients as common migraine ‘triggers.’ However, experimental research on the aggravating value of commonly reported food items and sensory conditions has not found any association between their exposure and the onset of migraine

(Karsan and Goadsby, 2018). This then brings up the question of whether such conditions are triggers or the early presentation of migraine such as changes in regulatory function and, or sensitivities to exogenous factors (Karsan and Goadsby, 2018).

Premonitory symptoms may be better understood with broad categories such as homeostatic or hormonal changes, mood, and cognitive symptoms, migrainous and sensory sensitivities and cranial autonomic symptoms (Karsan and Goadsby, 2018; Maniyar et al. 2014a). Karsan and Goadsby (2018) suggest these categories best describe common premonitory symptoms and the underlying pathophysiology. Karsan and Goadsby (2018) suggest homeostatic and hormonal changes may take the form of food cravings, yawning, thirst, and impaired sleep. Migrainous and sensory sensitivities typically involve stimuli such as light, sound and water; however, some patients also report neck pain or stiffness, and cutaneous allodynia (Karsan and Goadsby, 2018). Nausea may also be explained by this category. Cranial autonomic symptoms may include nasal stuffiness, impaired taste, rhinorrhoea and tearing eyes (lacrimation) (Karsan and Goadsby, 2018). Cognitive and mood symptoms during the prodrome typically include impaired concentration, memory, and mood changes (Karsan and Goadsby, 2018: p704).

Some research has commented on the lack of reliability of findings associated the prodrome phase of migraine and the role of hypothalamic dysfunction (Gollion et al., 2022). The authors of this review further highlight the lack of consistency across definitions of the prodromal phase, which limits comparison across studies (Gollion et al. 2022). For example, how long prior to the onset of pain constitutes the prodrome phase, which in turn determines what behaviours are captured across studies (Gollion et al. 2022). Further limitations are considered

regarding what constitutes symptoms of the prodromal phase and how many symptoms are required to be considered the presentation of the phase (Gollion et al. 2022). Gollion et al. (2022) further mention the lack of replication across samples. Experimental studies on animals have observed an association with hypothalamic neurotransmitters and neuropeptides in regulating trigeminal pain. This association, however, has not been observed in human samples (Gollion et al. 2022). In another systematic review and meta-analysis, Eigenbrodt et al. (2022) found that presence of a prodromal phase or premonitory symptoms varied greatly across studies with 66% of clinical samples experiencing at least one symptom compared to population-based studies where this frequency was much lower at 29%.

1.2.3 The Postdrome

Following the cessation of migraine pain, many individuals with migraine report persisting symptoms that may last up to 48 hours; research on migraine has defined this period as the postdrome. Similar to the prodrome phase, a wide array of symptoms may occur during this period, including neurological, psychological, sensory, physical, gastrointestinal, and whole-body symptoms (Bose et al., 2018; Bose & Goadsby, 2016). Bose et al. (2018) further classify these symptoms into four categories: neuropsychiatric, sensory, gastrointestinal, and general systemic symptoms. Neuropsychiatric symptoms include mood changes, changes in cognitive performance and disordered sleep patterns such as insomnia. Sensory symptoms include photophobia and phonophobia, among others (Bose et al., 2018). Gastrointestinal symptoms include but are not limited to nausea, vomiting, constipation, diarrhoea, food cravings, and stomach pain (Bose et al., 2018). Finally, Bose et al. (2018) include general systemic symptoms that comprise symptoms such as tiredness, polyuria and fluid retention. An electronic diary study by Giffin et al.,

(2016) found that in a sample of 120 migraineurs, 81% reported postdrome symptoms with tiredness, difficulty concentrating, neck stiffness, light sensitivity and irritability being the most frequent. Giffin et al. (2016), further found that migraine severity or medication taken was not associated with postdrome duration.

A study by Thuraiayah et al. (2024), observed that in a sample of 631 participants, 80.7% participants experienced at least one postdrome symptom when prompted versus 66.7% when not prompted. These findings may reflect the varying nature of the symptoms which may make recognising their association with the migraine attack difficult. The postdrome phase is the least studied of the migraine phases with particularly little research on the neurological underpinnings of the phase. However, a dissertation by Bose (2018) using arterial spin labelled magnetic resonance imaging found that during this phase, there was reduced cerebral blood flow (CBF) across frontal, temporal, insular, cingulate, and occipital brain regions in comparison to baseline, interictal conditions. Bose (2018) discusses the reduction of CBF in distinct conditions such as fibromyalgia where similar to the postdrome, fatigue is common. Bose (2018) suggests that observed reductions in CBF may be due to widespread vasoconstriction initiated by the brainstem or separately, cortical spreading depression. Bose (2018) further highlights the lack of activation in the hypothalamus during the postdrome versus the prodrome emphasising the distinction between these phases although the reported overlap in symptoms.

Table 1.2. Taken from Giffin et al. (2016), highlighting the percentage of participants from an electronic diary study who recalled specific prodromal symptoms at baseline alongside the percentage of symptoms recorded throughout the study period.

Non-headache feature	Percent of patients who recalled each postdromal symptom at baseline (n = 83)	Percent of attacks prospectively reporting each postdromal symptom during the e-diary study (n = 425)
Tired / Weary	75	88
Difficulty with concentration	67	56
Stiff neck	16	42
Light sensitive	13	36
Intolerant / irritable	22	29
Dizziness	10	19
Yawning	15	14
Pale face	18	21
Noise sensitive	12	32
Hunger / food craving	15	15
Thirst	13	32
Emotional	13	24
Difficulty with thoughts	15	33
Constipation	4	7
Frequent urination	7	21
Nausea / vomiting	6	15
Difficulty reading or writing	10	17
Difficulty with speech	5	9
Other	32	44

1.2.4. Differential Diagnosis

Common differential diagnoses for migraine however include primary headache disorders such as tension type headache and cluster headache. Furthermore, while there is anatomical overlap between migraine, cluster headache, and tension type headache; there are differences in the presentation of headache (Al-Karagholi et al., 2022; Onan et al., 2023). Tension type headache is characterised by bilateral pain that is distinguished by a pressure or tightness rather than pulsating qualities as observed in migraine (Eigenbrodt et al., 2021). The pain of tension-type headache further ranges from mild to moderate pain severity however this can last much longer than migraine with duration ranging from hours, weeks, or persisting indefinitely (Eigenbrodt et al., 2021). Diagnosis of tension-type headache does not require presentation of symptoms such as nausea or sensitivity to noise and light, but such symptoms may occur (Eigenbrodt et al., 2021). Similarly, unlike migraine headache, tension-type headache is not worsened by physical activity (Eigenbrodt et al., 2021). Cluster headache, while typically lasting no longer than three hours in duration, is distinguished by severe to very severe unilateral pain that is characterised as overwhelming (Eigenbrodt et al., 2021). Cluster headache is accompanied by autonomic symptoms, which present on the opposite side to the headache such as red eyes, tearing, or nasal congestion (Eigenbrodt et al., 2021: Table 1, p. 506). Medication overuse headache while not a primary headache disorder, is frequent among individuals with migraine occurring in up to 50% of patients and up to 2% in the general population (Gosalia et al., 2024). Medication over-use headache is defined by 15 or more headache days per month for a period of at least 3 months in a patient with a pre-existing headache disorder alongside regular overuse for >3 months of one or more drugs that can be taken for acute and/or

symptomatic treatment of headache (Gosalia et al., 2024; IHS, 2018). If specific medication overuse, such as ergotamine's, triptans, non-opioid analgesics (paracetamol, non-steroidal anti-inflammatory drugs) or opioids can be identified, a substance-specific medication overuse diagnosis is given; for example, ergotamine-overuse headache (IHS, 2018). Further, Gosalia et al. (2024), comment on the difficulty in differentiating headache caused by migraine or medication overuse in individuals with chronic migraine, highlighting the similarity in headache presentation.

1.2.5. Epidemiology of Migraine

Recent estimates indicate that migraine affects approximately 15% of the global population and accounts for 4.9% of total years lived with disability worldwide (Abdollahi et al., 2024; Steiner & Stovner, 2023). Chronic migraine is estimated to occur in 1.4-2.2% of the general population, or approximately 8% of migraine diagnoses (Ashina et al., 2021; Buse et al., 2012; Natoli et al., 2010). The prevalence of migraine with aura versus migraine without aura is not clearly established in the literature, with epidemiological studies in migraine being quite a recent development in the research (Steiner & Stovner, 2023). As well as this, prevalence varies between studies, due to a number of factors such as outdated diagnostic criteria, different sampling methods, and general demographic variance due to sex, age and geography (Rasmussen & Olesen, 1992; Stovner et al., 2022). The incidence of migraine was estimated at 86.7 million new cases in 2019—an increase of about 40% since 1990 (Fan et al., 2023). However, this rise reflects global population growth rather than an increase in individual risk (Fan et al., 2023). Incidence typically peaks in adolescence and young adulthood, particularly among

females, and declines with age (Fan et al., 2023). Prevalence is also strongly influenced by sex, with migraine being around three times more common in females than in males (Lebedeva, 2022). Moreover, attacks in females tend to be more symptomatic and of longer duration (Verhagen et al., 2023). These sex differences are thought to be a result of fluctuations in sex hormones, such as oestrogen and progesterone, which affect neural and vascular mechanisms implicated in migraine pathophysiology (Allais et al., 2020). Migraine incidence has been shown to increase during the onset of hormonal events in females such as puberty, pregnancy and menopause (Amiri et al., 2022). The importance of sex hormones in female migraine is reinforced by research that suggests resolution of migraine in approximately 50% of women over the age of 50, following menopause; this percentage increased with age (Bugge et al., 2025). Prior to this, some research suggests that migraine burden increases between the ages of 30 and 40 years (Safiri et al., 2022). However, cessation of migraine is not consistent, and migraine can persist in older populations over 60 years although incidence and prevalence are significantly reduced (de Rijk et al., 2018).

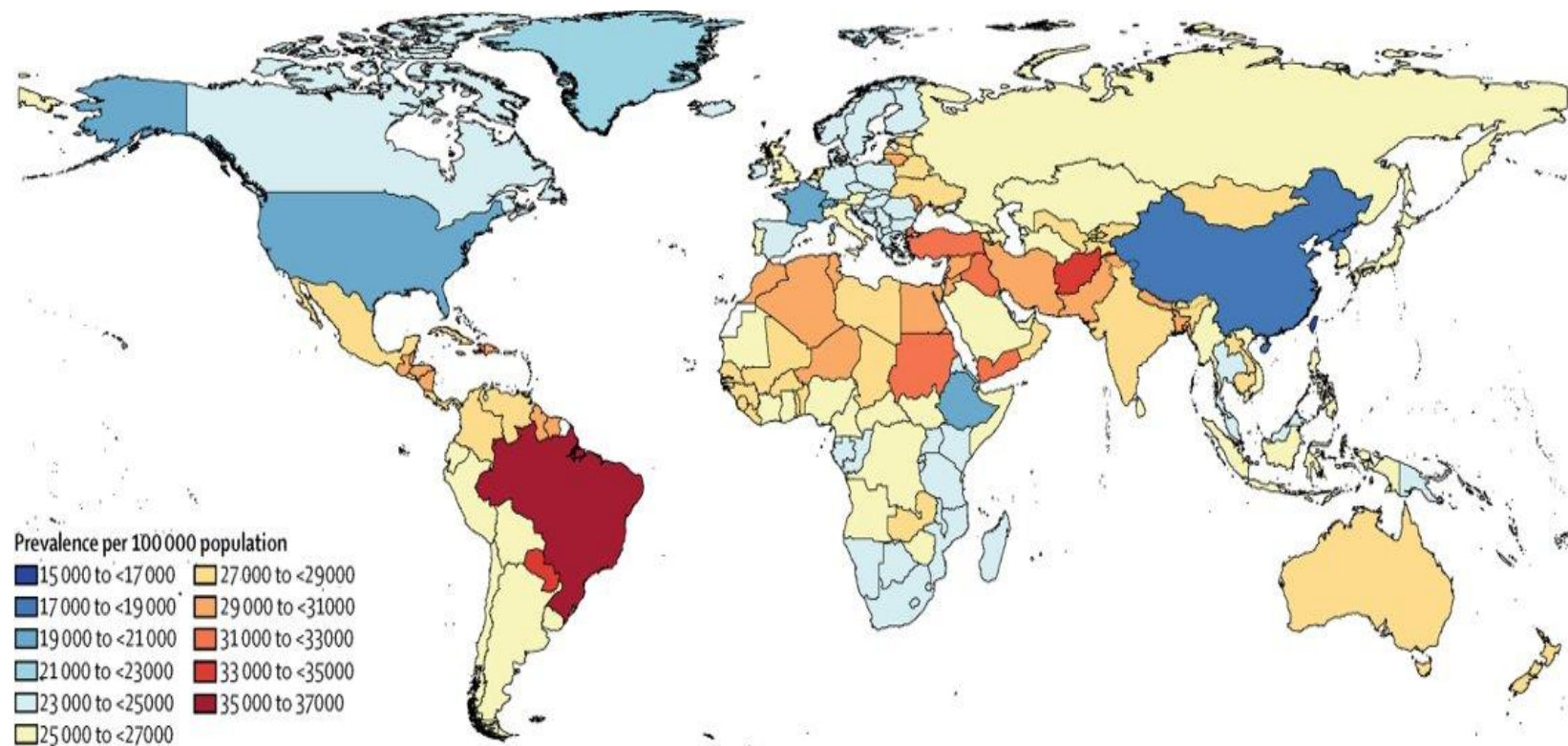


Figure 1. 1. Figure adapted from the Global Burden of Disease Headache Collaborators (2016) highlighting the global prevalence of migraine with Republic of Irelands prevalence estimated to be between 23,000 and 25,000 cases per 100,000 of the population.

1.2.6. Migraine as a Vascular Disorder

Only in the last decade has it become evident that migraine is a neurological disorder rather than vascular pain condition. Prior to this it was believed that dilation of the cranial arteries was the cause of migraine pain experienced effectively defining the condition as another ‘headache’ (Amin et al., 2013; Ray & Wolf, 1940). As such the pathophysiology of migraine was thought to be the same as headache associated with pyrexia (fever) and hypertension (Ray & Wolff, 1940). Using a sample of 30 surgical patients who had undergone cranial surgery which exposed the sub cranial anatomy, Ray and Wolff (1940) examined the pain sensitivity of the scalp, galea, fascia and muscle. Observations from these experiments highlighted that, participants reported increased pain sensitivity of cranial arteries with increasing proximity to the galea and noted overall increased sensitivity of the fascia and respective muscles (temporal and occipital) (See Ray and Wolf, 1940, p:816). The epicranium was found to be less sensitive and insensitive in some places, including the vertex. Pain sensitivity increased mildly over the brow bone and in the low temporal and occipital regions, with more moderate pain in the base of the skull. All extracranial arteries of the scalp were found to induce pain when stimulated whereas veins were found to be less sensitive. The external carotid artery and its branches (occipital and postauricular) were further found to be sensitive to pain. Stimulation of the cranial arteries such as the occipital arteries, the supraorbital and frontal arteries and the superficial temporal artery induced ipsilateral pain. Regarding the intracranial structures, the great venous sinuses associated tributaries brain surface to parts of the dura at the base, the dural arteries and the cerebral arteries at the base of the brain were found to be sensitive to pain inducing stimulation. In the cranium, the parenchyma and nerves were the only structures that were sensitive to

pain. Furthermore, Ray and Wolff (1940; p:856) proposed the following hypotheses of the underlying mechanisms necessary for pain onset in migraine;

Tension exerted on the veins connecting to the venous sinuses from the cerebral surface, leading to displacement of the major venous sinuses; tension on the middle meningeal arteries, major arteries at the brain's base and their primary branches; the expansion and dilation of intracranial and extracranial arteries; inflammation within or surrounding any pain-sensitive structures within the head; and direct compression by tumours on the cranial and cervical nerves housing numerous pain-conveying fibres from the head (Ray and Wolff, 1940; p:856).

Tunis & Wolff (1953) found that migraineurs experienced increased pulsation of the superficial temporal artery while experiencing migraine pain, supported and propelled the notion of migraine as a vascular pain disorder. More recent studies, such as that by Amin et al. (2013) found that during a migraine, there was no significant change in the extracranial arteries in accordance with the side of pain however the intracranial arteries were significantly more dilated. Both intracranial cerebral and cavernous parts of the carotid artery and the middle cerebral artery displayed statistically significant dilation during the migraine compared to interictally; however, this difference was small (Amin et al., 2013).

The role of vasodilation, and the vascular nature of migraine, was further supported by the effective use of vascular medications such as calcitonin gene-related peptide receptor (CGRP) antagonists and triptans. One of the functions of CGRP is that of a potent vasodilator and CGRP antagonists work by blocking CGRP from binding rather than working as a vasoconstrictor (Russo & Hay, 2023). CGRP has been noted by Russo and Hay (2023) to be a complex peptide which research has

only began to understand, however it is evident that it is expressed across the central and peripheral nervous systems including various brain regions that are important for migraine pathology including the cerebellum, thalamus, hypothalamus and brainstem (Russo & Hay, 2023). The current understanding of CGRP highlights the importance of the peptide in potential migraine pathology such as in vasodilation, pain signalling, and peripheral sensitisation (Russo & Hay, 2023). Furthermore, Russo and Hay suggest that elevated levels of CGRP may be expressed in migraine in response to changes in blood vessels via the trigeminovascular system or cortical spreading depression. As such the elevated levels of CGRP may trigger a sensitisation response. Russo and Hay (2023) suggest that this sensitisation response may form a feedback loop which may explain the experiences of pain and sensitivity to light and noise observed in migraine. As such the role of CGRP in migraine helps to shed light on the multitude of potential mechanisms behind migraine pathology including inflammation, vascular disorder, and sensory hypersensitivity.

1.2.7. Moving Away from the Vascular Theory of Migraine

The move away from the vascular theory of migraine is credited to Jensen and Olesen commonly referred to as the Norwegian group (Jensen, 1987; Jensen & Olesen, 1985; Olesen et al. 1990). Jensen and Olesen (1985) externally examined temporal muscle blood flow using the ¹¹³-Xenon washout technique and observed no significant change in median blood flow to the contra and ipsilateral sides. Furthermore, no association between migraine and changes in muscle tension as measured by electromyography was observed. A second study by Jensen (1985) further observed comparable results using the ¹¹³ Xenon washout technique. In this study, no significant differences were observed in mean arterial blood pressure

during and between attacks (Jensen, 1985). Similarly, no significant difference in orthostatic increase in heart rate was observed during and between attacks.

Enabled by the advancements in technology, Olesen et al. (1990) examined intracerebral vasodilation during a spontaneous migraine attack using single-photon emission tomography. In this study, Olesen et al. (1990) observed reduced regional cerebral blood flow during the headache phase and gradually increased during this phase and persists after the pain has ceased. In such cases the intracerebral arteries were constricted during and following the onset of the headache phase. The change in rCBF further did not affect the manifestation of headache and the characteristics of the pain experienced (Olesen et al., 1990). Olesen et al. (1990) further suggest migraine to be associated with the biological underpinnings associated with reduced regional cerebral blood flow. Changes in cerebral blood flow may further be specific to individuals diagnosed with migraine with aura. Research by Sanchez del Rio (1999) observed reduced cerebral blood flow in the occipital lobe in migraineurs with aura, while no significant changes were observed in those without aura. Changes in rCBF that were observed by Olesen et al. (1990) were in non-nociceptive brain areas previously examined by Ray and Wolf (1940). Olesen et al. (1990) further suggest that any subsequent observed increases in blood flow and vasodilation are secondary symptoms with no involvement with the mechanisms behind migraine pain.

Administration of vasoactive substances is not always effective in inducing migraine. A study which administrated individuals with' vasoactive intestinal peptide (VIP) did not induce a migraine attack (Rahman et al. 2007 in Ho et al., 2010). Furthermore, while there has been some success in aborting migraine pain using CGRP antagonists and Triptans, the role of vasodilation and inflammation has been

challenged as other vascular and inflammatory drugs have not been effective in treating migraine (Ho, Edvinsson & Goadsby, 2010). Such findings suggest that vasodilation is not necessary in migraine induction however it may coincide with the onset.

1.2.8. Migraine as a Neuro-Inflammatory Disorder

Some researchers have argued for the role of neurogenic inflammation in migraine as the key mechanism in triggering the headache phase (Kursun et al., 2021). Neuroinflammation, not unlike inflammation elsewhere in the body, is a physiological immune response to harmful stimuli and environmental factors such as pathogens or infections, trauma, and general stress. The inflammatory response enables the harmful factor to be localised and removed or allows for adaption (Medzhitov, 2008). With regard to migraine, three types of inflammatory processes have been described. Typical inflammation marked by changes in tissue regarding colour, temperature, swelling and pain. Molecular and cellular markers of inflammation include cytokines, histamines and leukocytes and mast cells respectively (Charles et al., 2021). Neurogenic inflammation is caused by nociceptor activation which causes the release of neurotransmitters and subsequent plasma extravasation (Matsuda et al., 2019). Neuroinflammation however refers to localised inflammatory responses in the peripheral and central nervous systems (Matsuda et al., 2019). Neuroinflammation is characterised by glial cell activation, increased vascular permeability, leukocyte infiltration, and the production of inflammatory mediators such as cytokines which cause sensitisation (Matsuda et al., 2019).

It has been suggested that activation of the meningeal perivascular trigeminal nociceptors by compounds such as potassium which signal to pain processing areas in migraine can simultaneously cause inflammation in the dura matter (Kursun et al.

2021) Similarly, signals from perivascular neurons which signal the release of vasoactive inflammatory mediators (Kursun et al. 2021). Levels of pro and anti-inflammatory cytokines are further increased during an attack suggesting a role of neuroinflammation. Cortical spreading depolarisation may further function to initiate migraine through neuroinflammatory signalling in migraineurs with aura (Kursun et al. 2021; Thompson and Hakim, 2005). CSD may act as a protective mechanism against ischemic injury. Research using animal models such as rats found that levels of damage following cerebral ischemic events were significantly reduced in those who had been subjected to cortical spreading depression compared to controls (Matsushima et al., 1996). The administration of inflammatory soup to rodents has further highlighted activation and sensitisation of the trigeminovascular neurons for an extended period of time (Goadsby et al., 2017). Sensitisation of trigeminovascular neurons further causes hypersensitivity of the dural vasculature (Goadsby et al., 2017).

Animal studies using rodents such as rats have tried to demonstrate the role of inflammatory processes in migraine onset through administering nitro-glycerine a known chemical migraine trigger, which causes the delayed release of inflammatory agents that then work to sensitise pain receptors located in the meninges of the rodent brain (Goadsby et al. 2017). Administration of nitro-glycerine further increases the production of nitric oxide synthase in the dura mater causing protein expression and plasma protein leakage which may be prevented by inhibiting nitric oxide synthase. Plasma extravasation is a process that occurs during inflammation, where blood vessels become more permeable allowing plasma to diffuse into surrounding tissues. Experimental research inhibiting nitric oxide synthase however has not been sufficient or, successful in migraine prevention or treatment alongside

other treatments that target plasma extravasation. Furthermore, administration of CGRP to induce migraine (which enables immune cells to reach the site of inflammation) further did not induce dural plasma protein extravasation in rats, a key feature of neurogenic inflammation (Goadsby et al. 2017). Similarly, Edvinsson et al. (2019) have suggested that the lack of inflammatory markers of the central nervous system such as glial cell activation, leukocyte infiltration or changes to the blood brain barrier point away from CNS inflammation. Such findings point away from a neuronal inflammation pathophysiology in migraine onset (Goadsby et al. 2017). The potential role for neurogenic inflammation through activation of trigeminal sensory pathways causing an inflammatory response through reoccurring release of neurotransmitters and neuropeptides however needs to be explored further (Edvinsson et al., 2019).

1.2.9 Migraine as a Neurological Disorder of Sensory Thresholds

Migraine has three major phases. The premonitory phase which precedes causing fatigue, poor mood, or impaired concentration; head pain and increased sensitivity to sensory stimuli in the headache phase, and the lasting tiredness and unwell experienced in the postdrome following the attack (Goadsby et al, 2017; Green & Muskin, 2013; Qubty & Patniyot, 2020). Brain imaging studies have found increased regional cerebral blood flow in brain areas including the posterior hypothalamic region, the thalamus, the periaqueductal grey region, the dorsal pons, and the brainstem in migraine patients (Goadsby et al, 2017; Maniyar et al, 2014).

Previous research on migraine has highlighted the role of cortical spreading depression, activation of the trigeminovascular system or hyperexcitability of the cortex, however absolute mechanisms remain largely unknown (Goadsby et al, 2017; Hargreaves, 2007; Qubty & Patniyot, 2020). Research combining structural and

functional imaging on the brain suggest migraine to be related to the dysregulation of sensory processing (Goadsby et al, 2017).

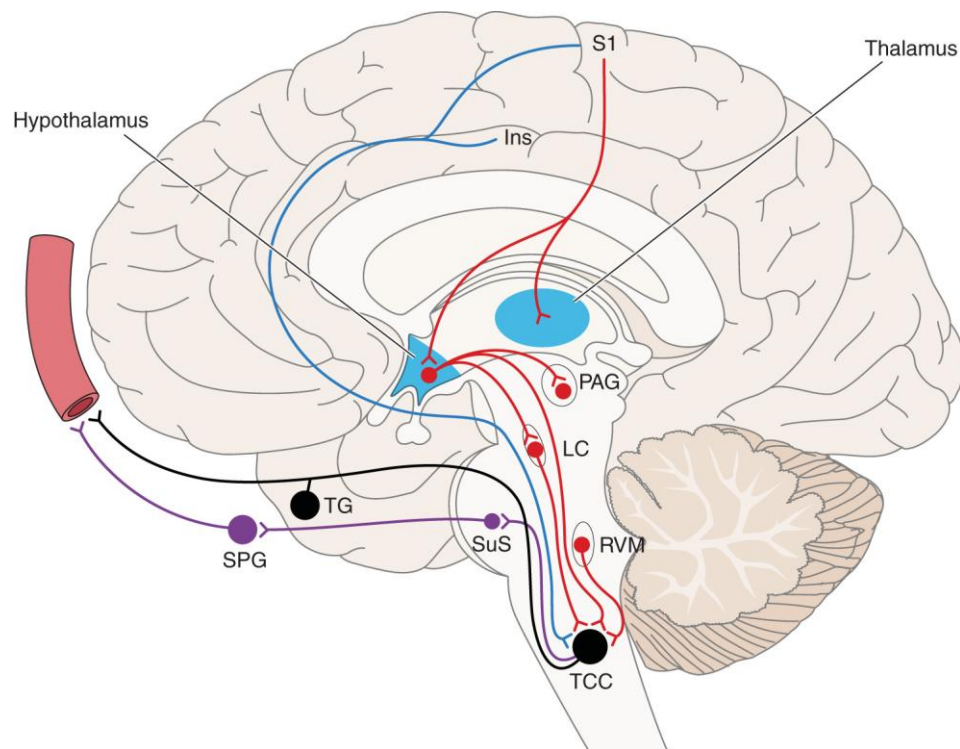


Figure 1. 2. Diagram taken from Goadsby et al. (2017) illustrating the direct and indirect descending pathways from cortical structures to the trigeminovascular system. Indirect projections from the somatosensory cortex (S1) terminate in the thalamus and hypothalamus, while additional signals from S1 and the insular cortices project directly to the trigeminocervical complex (TCC). The hypothalamus sends further projections to the periaqueductal gray area (PAG) and to the TCC both directly and indirectly via the locus coeruleus (LC). Descending input from the rostral ventral medulla (RVM) also reaches the TCC. Outputs from the TCC project to the superior salivatory nucleus (SuS), which in turn connects to the sphenopalatine ganglion (SPG), with a secondary projection linking the TCC to the trigeminal ganglion (TG). Together, these descending pathways relay cortical information to the trigeminovascular system, and its nerve endings located extracranially in the face and scalp and intracranially in the dura mater and meningeal blood vessels.

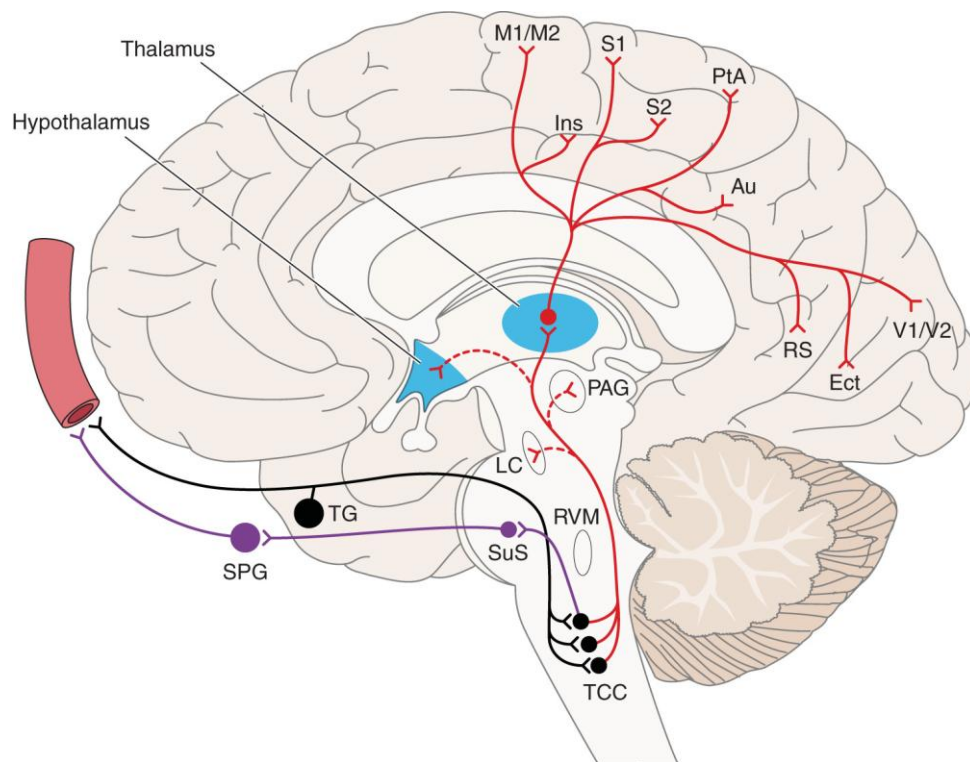


Figure 1.3. Functional imaging studies have further highlighted that migraineurs are more sensitive to sensory stimuli and show increased activity in various sensory modalities of the brain between attacks (Boulloche et al, 2010; Demarquay et al, 2008; Goadsby et al, 2017; Vanagaite et al, 1997). Imaging research by Meylakh and Henderson (2022) observed increased infra-slow oscillatory activity in the primary, secondary and third visual cortices of migraineurs in comparison to controls. Further inspection of resting connectivity found that migraineurs in the study displayed greater connectivity between V1 and V2 with the auditory, motor, gustatory and somatosensory cortices (Meylakh and Henderson, 2022).

Various neuroimaging studies have further observed structural differences in the migraine brain. Such studies have found reduced grey matter in brain areas involved in processing pain (Goadsby et al., 2017; Qin et al., 2019). Structural differences in the cerebellum and brainstem have further been observed in migraineurs without aura in comparison to healthy controls using voxel-based morphometry and diffusion tensor imaging (Qin et al. 2019). The right inferior cerebellum peduncle tract and spinal trigeminal nucleus in the migraine group displayed greater axial, mean and radial diffusivity (Qin et al, 2019). Research on migraine has further observed reduced activation of the spinal trigeminal nucleus (STN) between migraine attacks in comparison to non-migraine controls. The STN is involved in relaying sensory information from the face to the cortex. Activation of the STN signals the release of neuropeptides such as Calcitonin Gene Related Peptide (CGRP), substance P, vasoactive intestinal peptide, neurokinin A, nitric oxide synthase, and pituitary adenylate cyclase activating polypeptide (Waliszewska et al., 2021). The role of CGRP as a neuropeptide is that of a significant vasodilator and regulation of second and third order pain neurons (Puleda et al., 2023).

Increased levels of CGRP have further been observed to be associated with reduced inhibitory mechanisms which in turn may increase the sensitivity of the cortices involved in migraine (Ho et al., 2010; Puleda et al., 2023). It has been suggested that similar to the mechanisms observed in epilepsy, the peripheral trigeminovascular neurons are sensitised which spreads and causes the sensitisation of the nucleus caudalis, cervical spinal cord, thalamus, medulla, brainstem, and diencephalic regions (Ho et al., 2010; Puleda et al. 2023).

Findings by Stankewitz et al. (2011) found that this deactivation of the STN displayed cyclic behaviour over the course of a migraine attack with an increase in

activation prior to attack compared to interictal states. Activation of the STN significantly reduced during the migraine attack. This increase in activation of the STN significantly predicted the onset of a migraine attack (Stankewitz et al., 2011). The importance of the STN has further been demonstrated through the development and use of Calcitonin Gene Related Peptide inhibitors in pharmaceutical migraine treatments which receptors lay in the STN of the brainstem (Eftekhari & Edvinsson, 2011).

Similarly, using functional magnetic resonance imaging, research by Meylakh et al. (2021) observed an increase in resting state brainstem variability 24-hours prior to the onset of migraine. Further animal studies have further indicated the importance of the brainstem in initiating changes in brain functioning during an attack. The internal structures of the brainstem such as the locus coeruleus, rostral ventral medulla, superior salivatory and cuneiform nucleus are further known to be involved in trigeminovascular pain and autonomic control. These areas are further targeted pharmacologically using common migraine treatments such as triptans and CRGP antagonists (Puledda et al. 2023)

The ventral tegmental parabrachial pigmented nucleus (VTAPBP) modulates nociceptive information in the rat model including glutamate, naratriptan, pituitary adenylate cyclase activating polypeptide and dopamine. The VTAPBP further is implicated in eating behaviours as it plays a role in hedonic feeding, eating to fulfil a need for pleasure rather than hunger (Puledda et al. 2023). As such Puledda et al. (2023) suggests that potential cravings and triggers commonly reported prior to migraine onset may be early presentations of the prodrome further explaining the lack of support for aggravating factors or triggers in experimental studies. Puledda et al. (2023, p.3655), suggest that activation of these trigemino-parabrachial-limbic

networks may explain the “affective-motivational” symptoms of migraine.

Ultimately, while the pathophysiological mechanisms underlying the initiation of migraine remain unclear, it is now widely accepted that these mechanisms are neurological and involves the trigeminovascular system and its projections to various cortical areas and vascular systems, with vascular changes being insufficient to initiate the attack but occasionally coinciding with the headache stage.

1.2.10 Metabolism in Migraine

Research on metabolic functioning in migraine has suggested an intrinsic connection between migraine and energy metabolism. Experimental and clinical studies have suggested a role for an energy deficit and mitochondrial dysfunction in the disorder (Cavestro et al., 2025; Grech et al., 2022; Gross et al., 2019). Coinciding with previous studies that suggest a role of sensitisation, migraine research investigating metabolic functioning proposes that a lack of habituation or increased sensory reactivity, coupled with a reduced energy reserve, may act to trigger the trigeminovascular system (Cavestro et al., 2025; Grech et al., 2022; Gross et al., 2019). Furthermore, neural functioning in migraine is likely to be more energy intensive due to the greater reactivity and reduced habituation observed in this (Cavestro et al., 2025; Grech et al., 2022; Gross et al., 2019).

F-fluorodeoxyglucose positron emission tomography has further demonstrated greater glucose uptake in the occipital lobes interictally in migraineurs without aura compared to healthy controls, indicating persistent metabolic alterations (Gross et al., 2019). Links between metabolic functioning and migraine are further observed when considering common prodromal symptoms, including changes in appetite, sleep, exercise, and hormonal fluctuations, all of which reflect underlying metabolic regulation (Cavestro et al., 2025; Gross et al., 2019). Further, research has

observed significant correlations between reduced cerebral energy metabolism and migraine frequency (Cavestro et al., 2025; Grech et al., 2022; Gross et al., 2019). Gross et al. (2019) propose that migraine may represent an adaptive behavioural response to insufficient energy availability in the brain, potentially accounting for symptoms observed during the prodromal phase. Additional studies have reported increased lipolysis and ketogenesis during ictal and interictal stages, which may reflect compensatory responses to an energy deficit and reduced insulin availability, thereby providing secondary energy substrates for the (Cavestro et al., 2025; Grech et al., 2022; Gross et al., 2019). Gross et al. (2019) further discuss the potential role of oxidative stress, with elevated free radical production following oxygen metabolism in migraine. Consistent with this, reduced metabolic markers including interictal phosphate, ATP, and cytosolic free magnesium have been reported in migraine, alongside phosphorus magnetic resonance spectroscopy evidence of impaired mitochondrial oxidative phosphorylation during both ictal (during a migraine headache) and interictal (between migraine headaches) phases (Cavestro et al., 2025; Grech et al., 2022; Gross et al., 2019).

1.2.11 Final Thoughts on The Mechanisms of Migraine

Migraine has a significant impact on global health, with approximately 15% of the global population diagnosed with migraine, accounting for 4.9% of total years lived with disability worldwide (Abdollahi et al., 2024; Steiner & Stovner, 2023). Even with its high prevalence and burden, the complexity of migraine is evident throughout the literature on the condition, with research examining various aspects of migraine, and through different disciplinary lenses. Migraine, which was once known as a headache, a chronic pain condition, has been investigated as a vascular disorder, a sensory disorder, a metabolic disorder, a neuro-inflammatory disorder

and a neurological disorder (Amin et al., 2013; Cavestro et al., 2025; Goadsby et al., 2017; Grech et al., 2022; Gross et al., 2019; Kursun et al., 2021; Puledda et al., 2023; Ray & Wolf, 1940). The migraine literature is ever-changing, with current research suggesting the possibility of dysregulation prior to the onset of pain, questioning the role of aggravating factors or ‘migraine triggers’ and the presence of prodrome and postdrome phases (Karsan & Goadsby, 2023). It is likely that all of the above is true. While the current state of the literature situates migraine as a neurological disorder due to abnormal plasticity, it also consists of sensory, vascular, inflammatory and metabolic abnormalities (Amin et al., 2013; Cavestro et al., 2025; Goadsby et al., 2017; Grech et al., 2022; Gross et al., 2019; Kursun et al., 2021; Puledda et al. 2023; Ray & Wolf, 1940).

1.3 Sleep and Circadian Rhythms

1.3.1. Sleep

Sleep is conceptually difficult to define. Irwin (2019) describes sleep as a “naturally recurring state of arousal of the brain and body, which is behaviourally characterised by altered consciousness, decreased responsivity to stimuli and the inhibition of voluntary movement” (p. 703). Furthermore, sleep is a state marked by collective changes in functioning to when we are awake. The changes in functioning at the neuronal level were first observed by early research which investigated neural activity during sleep using electroencephalography (Loomis et al., 1937).

Electroencephalography uses electrodes which can measure electrical activity such as voltage in the brain corresponding to post-synaptic potentials of neuronal signalling (Loomis et al., 1937). This study found that electroencephalography (EEG) detected fluctuations in electrical potential over the course of the sleep period,

with corresponding changes in wave amplitude and frequency that marked transitions between distinct sleep stages (Loomis et al., 1937). Loomis et al. (1937) proposed five distinct stages based on their recordings. Furthermore, classification of sleep in the second half of the 20th century suggested that the five stages consist of four stages of non-rapid eye movement sleep (NREM) and one stage of REM sleep that are repeated over the sleep duration (Kales & Rechtschaffen, 1968). However, due to the qualitative similarity of the 3rd and 4th stages as slow wave sleep these stages were combined leaving the stages of NREM sleep to be classified as N1, N2 and N3 with N3 being slow-wave sleep and the REM stage of sleep as R (Moser et al., 2009).

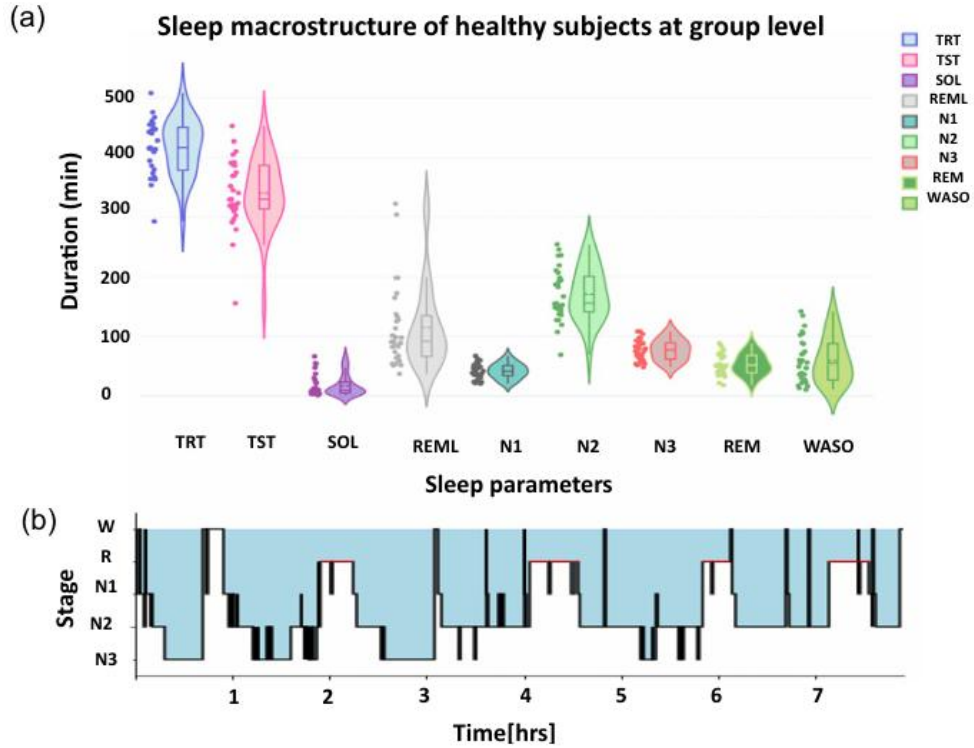


Figure 1. 4. Taken from Wei et al. (2024). (a) Violin plots of the average and range of sleep parameters in a healthy adult sample including total record time (TRT), total sleep time (TST), sleep onset latency (SOL), rapid eye movement latency (REML), N1, N2, N3, rapid eye movement (REM), wake after sleep onset (WASO). (b) Hypnogram of a healthy adult male which depicts the cycling through sleep stages over the sleep duration (hours).

The first stage, N1, acts as a transitional stage in sleep and is the first stage of sleep, it is the lightest stage of sleep where the individual is easily awoken. This stage is characterised by low amplitude mixed frequency activity in the theta range (Lambert & Peter-Derex, 2023). The second stage, N2, is comprised of deeper sleep with reduced heart rate and body temperature and EEG recordings of sleep spindles which are brief potentials measuring between 10-15 Hz (Andrillion et al., 2011) and high amplitude delta waves called K-complexes (Patel et al., 2024). The third stage,

N3 is defined by slow waves of between .5 and 2 Hz frequency (Lambert & Peter-Derex, 2023). Following N3, stage R, REM sleep defined by mixed frequency EEG, absence of sleep spindles and K complex, rapid eye movements measured by electrooculography and reduced muscle activity of the chin recorded by electromyography (Lambert & Peter-Derex, 2023).

The function of NREM sleep is suggested to be important in recovery at a cellular level and enables information processing and synaptic plasticity with the REM stage acting to test and modulate neuronal connections (Vyazovskiy & Delogu, 2014). However, the function of REM sleep is not determined, with other research suggesting it to have a significant role in memory such as consolidation of procedural memory, modulating and forgetting declarative memory (Mukai & Yamanaka, 2023). Alongside this, research has proposed that REM mediates important regulatory functions such as regulation of eating behaviours, autonomic regulation, body temperature, stress responses and development of cortical connections and motor functions (Mukai & Yamanaka, 2003).

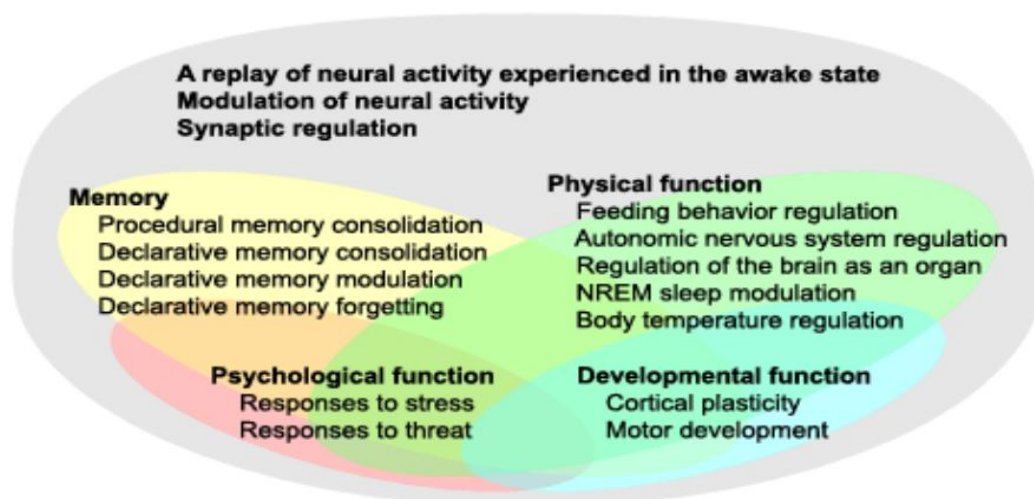


Figure 1. 5. Taken from Mukai and Yamanaka (2023) on the proposed functions of REM sleep in existing research.

Although the best way to measure sleep factors and sleep architecture (phases) is using polysomnography (PSG) which combines electroencephalography, electrooculography and electromyography as described above it is not an accessible method due to the large amount of equipment required and burden it places on participants. Sleep actigraphy using active watches which measure sleep onset, offset and duration can also be used to measure sleep timing and is a more accessible measurement of sleep in comparison to PSG method (Alakuijala et al., 2021; Conley et al., 2019). However, when assessing sleep staging, polysomnography is the only reliable method (Birrer et al., 2024). Research which utilises online, or remote designs may opt for alternative measures of sleep such as self-report questionnaires.

1.3.2. Circadian Rhythms

Evolutionarily, all organisms have been exposed to and shaped by both spatial and temporal environmental pressures. That is, the surrounding environment and the inherent time-based changes have selected for, or against, certain traits and behaviours (Pittendrigh, 1960). As such, since the 18th century research began to acknowledge the temporal fixation of certain behaviours across biological organisms (de Mairan, 1729). De Marian's (1729) experiment observed that the branches and leaves of the *mimosa pudica* plant move to face the sun, with the plant opening to maximise the area exposed to sunlight and closing at night. Furthermore, de Mairan (1729) noted that this was true even in the absence of light. However, it was not until the 20th century when research began explicitly on biological rhythms with experiments by Pittendrigh (1954;1960) in *drosophila* (fruit flies). Pittendrigh (1954) observed that the *drosophila* emergence from the pupusa maintained a 24-hour rhythm, across different temperatures in a controlled light-dark cycle of 12:12 hours. In a free-running phase of constant darkness the *drosophila* maintained the previously observed 24-hour rhythm (Pittendrigh, 1954; 1960). These findings

suggested the presence of an endogenous circadian rhythm of around (circa) a day (diem); 24 hours. Following this, Pittendrigh conducted a series of experiments in *Drosophila* and suggested that the circadian rhythm is endogenous, self-sustained, temperature compensated and can be entrained to environmental conditions or cues such as light exposure (Pittendrigh, 1960). Entrainment refers to the synchronisation of internal time with the external environment via entrainment cues known as zeitgeber or “time giver” (Roenneberg & Merrow, 2007). Light is by far the most important and widely understood zeitgeber in biological organisms including humans which may be entrained by various zeitgebers including as social cues (Aschoff et al., 1971; Roenneberg & Merrow, 2007).

Biological rhythms in mammals are governed by the master biological clock, the suprachiasmatic nucleus (SCN) (Moore & Eichler, 1972; Weaver, 1998). The SCN is in the anterior hypothalamus and above the optic chiasm and receives entraining information received through the retina and into the optic nerve (Antle & Silver, 2005). The SCN acts as a master pacemaker and synchronises the internal clocks all over the body, in organs and cells (Mohawk et al., 2013). However, aside from light input from the SCN, biological, non-photic zeitgebers such as peripheral and cellular oscillators too have a bidirectional synchronising effect with the SCN (Aschoff et al., 1971; Mistlberger & Skene, 2004; Mohawk, 2013; Roenneberg & Merrow, 2007). The mechanism by which the rhythms are entrained by the light cycle are due to ‘circadian cells’ within the retina (Roenneberg & Foster, 1997). The ‘circadian cells’ of the retina are intrinsically photosensitive retinal ganglion cells (ipRGCs) which contain the photopigment melanopsin (Brown & Robinson, 2009). These melanopsin-containing ipRGCs project non-visual light information to the suprachiasmatic nucleus via the retino-hypothalamic tract suggesting its role as a

circadian photopigment (Brown & Robinson, 2009). Research on photosensitive ipRGCs has shown that these cells are responsive to blue light and use this photic information to entrain the circadian cycle. When blue wave light is detected, light information is projected through the retino-hypothalamic tract to the SCN which then projects information to the pineal gland and suppresses melatonin secretion (Bailes & Lucas, 2009; Prayag, Najjar and Gronfier, 2019). In the same regard, blue light exposure at nighttime via artificial light sources and technology use has been shown to be related to delayed onset melatonin secretion (Prayag, Najjar & Gronfier, 2019).

The process by which input from the environment interacts with biological pacemakers is through a molecular transcriptional- translational feedback mechanism whereby the chronobiological basis of the rhythms is observed in genetic and cellular networks. Furthermore, while the suprachiasmatic nucleus is central to receiving light information and projecting to neural structures; there are numerous biological pacemakers within organs and bodily tissues via clock genes which enable cell autonomous time keeping via a transcriptional feedback loop (Takahashi, 2019). Genes such as circadian locomotor output cycles kaput (CLOCK) and brain and muscle aryl hydrocarbon receptor nuclear translocator-like 1 (BMAL1) are activating transcription factors which combine to form CLOCK-BMAL1 complex which binds to DNA to activate genes that exhibit a circadian rhythm including PER and CRY genes which encode repressor proteins that accumulate during the day and move to the nucleus at night to repress their own transcription (Takahashi, 2019, p. 166). When the PER and CRY repressor proteins are broken down, Clock-BMAL1 is no longer inhibited and is activated again the coming morning (Takahashi, 2019).

The sleep and wake cycle is the most directly observed and researched circadian behaviour. The light information received by the SCN determines the time when our body starts to biologically prepare for sleep and wake and the behaviour is easily observed (Roenneberg & Merrow, 2016). The timing and strength of light exposure can impact the internal time of the body, with light in the morning advancing the internal phase and light later in the evening or night causing a phase delay (Roenneberg & Foster, 1997). Due to genetic variation, the time of synchronisation with the external cue (light/dark) varies across individuals with some synchronising earlier or later in the 24-hour period than others, causing variation in time of sleep onset, offset and duration (Roenneberg et al, 2019). The variance of internal time between individuals can be categorised as temporal constructs or phenotypes of ‘normal,’ early, and late chronotypes (Roenneberg et al, 2019). Chronotype is a behavioural phenotype of circadian phase of entrainment, that is not only related to sleep but provides information on the variation of circadian rhythmicity of behaviours intrinsic to health such as sleep, diet, and patterned behaviour such as substance use (Roenneberg et al, 2019; Takahashi et al, 2018).

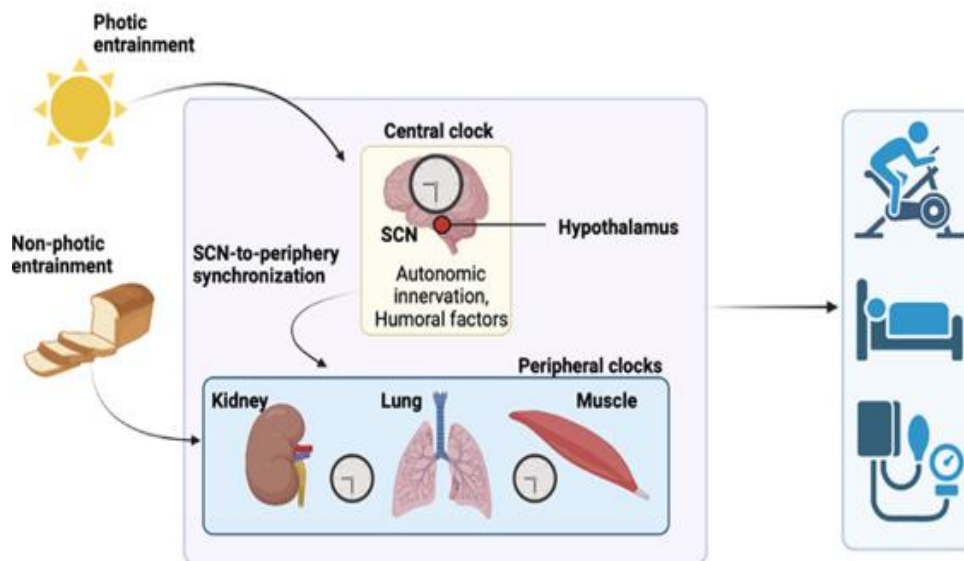


Figure 1. 6. Figure adapted from Crislip et al. (2021). Light signals are transmitted to the suprachiasmatic nucleus (SCN), synchronising the body’s peripheral clocks with the external light–dark cycle. Non-photic cues, such as feeding behaviour, also act to entrain internal circadian time. This entrainment regulates a range of internal biological processes not limited to metabolic function, immune activity, cardiovascular regulation, thermoregulation, cellular repair, and neural processes such as sleep–wake timing, as well as influencing external behavioural rhythms of activity and sleep.

1.3.3. Two Process Model of Sleep Regulation

The two process model of sleep regulation is a conceptual model that is widely accepted in sleep research to explain timing of sleep wake behaviour (Borbély, 2022). The two processes in the model are a homeostatic process (process S) and circadian process (process C) (Borbély, 2022). While the circadian process governs sleep-wake behaviour over a 24-hour day and is entrained partially by light dark cycles, the homeostatic process works via the need to sleep or ‘sleep pressure’ (Borbély, 2022). The longer an individual is awake, the more sleep pressure

accumulates to drive the individual to sleep. In the same regard, the circadian control of sleep and wake behaviours is enabled through the secretion of hormones throughout the day to maintain circadian arousal across the 24-hour cycle (Borbély, 2022). Circadian arousal is highest during the day and is at its lowest at night. The interplay between circadian arousal and sleep pressure regulates sleep behaviours as sleep is achieved when sleep pressure is high and circadian arousal is low (Borbély, 2022). The circadian aspects of sleep are sleep timing and rapid eye movement (REM) sleep whereas the homeostatic aspects, driven by sleep pressure is associated with slow-wave sleep during non-rapid eye movement sleep (NREM) which is responsible for restoration and recovery (Dijk & Archer, 2009; Vyazovskiy & Delogu, 2014).

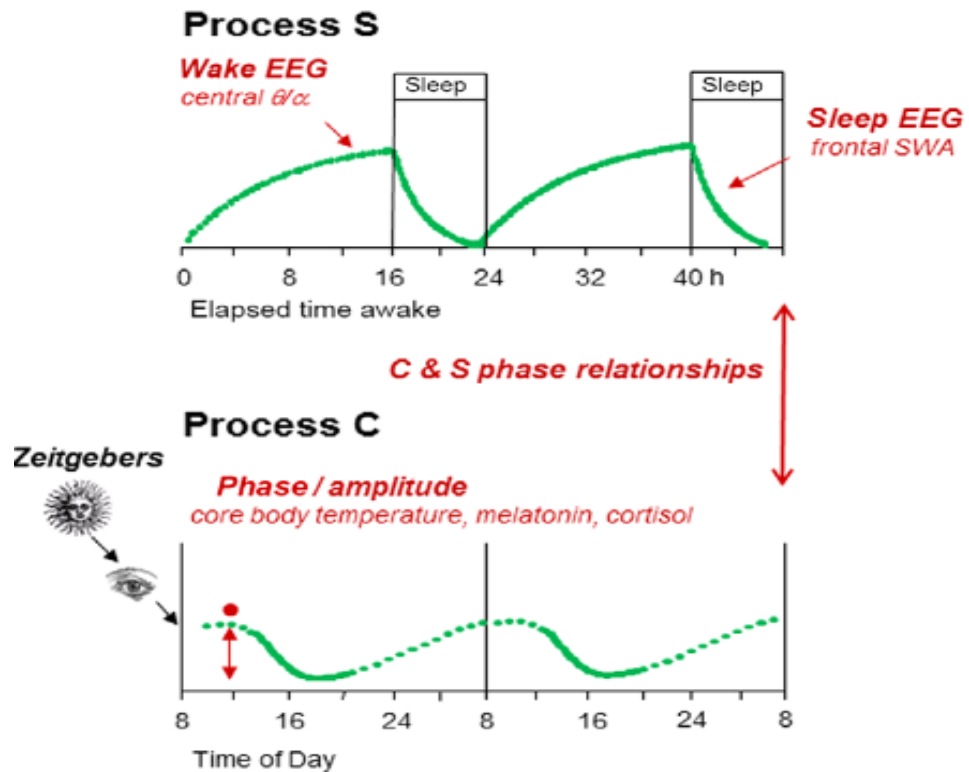


Figure 1. 7. Figure taken from Borbéley et al. (2016) of the two-process model of sleep where sleep pressure (process S) increases over time as the individual is awake and peaks before sleep onset which leads to a decline in sleep pressure. Alongside sleep pressure, circadian arousal (process C) peaks early in the morning and coincides with sunrise, and wakefulness and decreases throughout the day as sleep pressure increases.

1.3.4. Chronotype and the Munich Chronotype Questionnaire

The Munich Chronotype Questionnaire (MCTQ) is a useful tool and accessible measure of sleep timing and circadian phase of entrainment as the timing and individual goes to sleep is determined by the body's circadian clock (Roenneberg et al., 2003). The MCTQ asks participants to provide the time they go to sleep and wake up on workdays and work free days. Where individuals have social obligations such as work; sleep timing is no longer a reliable measure of

circadian phase, as the social clock determines the time the individual goes to sleep and wakes up (Roenneberg et al., 2019). From these values, several variables can be calculated including sleep duration on work and work free days, average weekly sleep duration, sleep loss and midsleep on free and working days. Midsleep on free days can be used as an indicator of circadian phase of entrainment (Roenneberg et al., 2003). However, if individuals are entrained to a later phase of entrainment, display a late chronotype, it is likely that individuals accumulate sleep loss as a result of not sleeping early enough on working days to account for the early wake up time required (Roenneberg et al., 2003; Roenneberg et al., 2007)). In these cases, a sleep correction to account for oversleep on free days to compensate for sleep loss accumulated over the working week is required. This variable is calculated as midsleep on free days sleep corrected (Roenneberg et al., 2007).

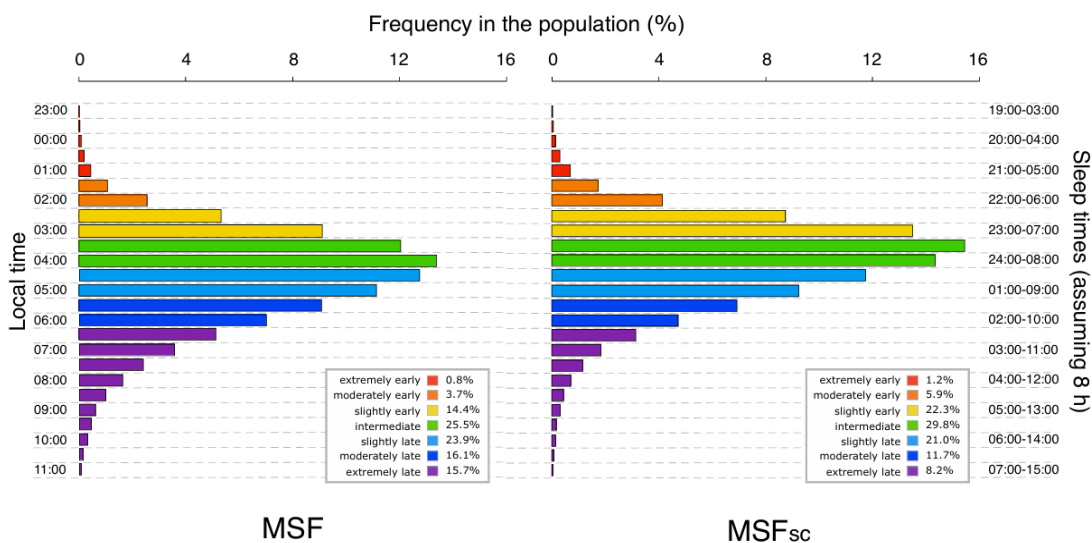


Figure 1. 8. Figure taken from Roenneberg et al. (2019) highlighting the distribution of midsleep on free days (MSF) and midsleep on free days sleep corrected (MSF_{sc}) in a large sample of participants taken from the Munich Chronotype Questionnaire Database. The right y-axis indicates MSF clock time values. The left y-axis indicates time of sleep onset and sleep end, assuming an eight-hour sleep duration.

1.3.5. Social Jetlag

Circadian rhythms interact with the social clock, the social world in which individuals' daily lives are scheduled (Roenneberg et al, 2019). With modernity, the social clock has become increasingly uncoordinated with the biological clock and that of the sun (Roenneberg et al, 2019; Roenneberg et al, 2007; Roenneberg et al, 2003). Social jetlag refers to such misalignment or discrepancies between individuals' circadian rhythms and the social clock (Roenneberg et al, 2019). Social jetlag can be calculated from the difference between midsleep on free days and midsleep on workdays (Roenneberg et al., 2019). Social jetlag is a predictor of various poor health outcomes such as obesity, diabetes and compromised cardiovascular health and headache (Cho et al, 2019; Roenneberg et al, 2012; Scheer et al, 2009). Social jetlag is typically greater in late chronotypes and more generally shift workers due to varying sleep patterns and accumulation of sleep debt as a result of the misalignment of the circadian clock with social obligations (Hulsegge et al, 2019; Roenneberg et al, 2019; Castilhos Beauvalet et al, 2017; Roenneberg et al, 2012; Sack et al, 2007; Wittmann et al, 2006).

1.3.6. Circadian Misalignment

The discrepancy between social and biological clocks is not the only form of circadian misalignment. Rather, various causes of misalignment between the internal and external time exist that the average individual may be exposed to at some point or another. Such causes of misalignment include crossing multiple time zones while flying; often referred to as jetlag (Ahmed et al., 2024). Jetlag is a temporary state of misalignment and often resolves itself after a couple of days of synchronising to the destinations external time (Roach & Sargent, 2019). Exposure to artificial light after

dark, is another modern cause of circadian misalignment of which various poor health outcomes have been shown to be associated with. Light emitted from artificial lighting and technology such as televisions and smartphones at night can delay melatonin secretion and delay sleep onset (Davis et al., 2023). Similarly, while circadian rhythms influence behaviour, behaviour also influences the rhythms. In this way, eating at night work to inform the body's circadian rhythms impacting not only on the sleep-wake cycle but more peripheral circadian processes such as metabolism (Pickel & Sung, 2020).

1.3.7. Sleep Duration and Quality

While not a circadian component of sleep, sleep duration is another important sleep factor in determining overall sleep quality and health outcomes whereby insufficient and excessive sleep have adverse effects on health (Cappuccio et al., 2010). For example, a study by Buxton and Marcelli (2010) found that insufficient sleep duration of less than 7 hours per night was associated with greater risk of obesity and hypertension in comparison to diabetes and cardiovascular disease which were associated with sleep duration over 8 hours per night (Buxton & Marcelli, 2010). Disrupted sleep is further associated with poor health outcomes and is significantly associated with all-cause mortality (Medic et al., 2017).

Measures of subjective sleep quality are useful in capturing a general level of sleep quality as perceived by the participant. Research investigating the relationship between objective and subjective sleep quality has shown that subjective sleep quality measures are associated with sleep duration and efficiency and is better explained by self-reported sleep variables rather than polysomnography or actigraphy (Cudney et al., 2022). Furthermore, while discrepancies in sleep may be highlighted from objective measurements, it does not necessarily translate to

subjective sleep quality (Cudney et al., 2022). Rather, research has found that objective measures explain more variance in subjective sleep quality within-subjects rather than between (Hachenberger, 2025). Self-reported sleep quality questionnaires are also more accessible to researchers and participants (Fabbri et al., 2021).

Significant impairment of sleep may warrant diagnosis of a sleep disorder. Sleep disorders are typically categorised as dyssomnias or parasomnias (Ohayon, 2011; Petit et al., 2007). Dyssomnias impact the amount, quality or timing of sleep and include disorders such as insomnia, narcolepsy, obstructive sleep apnoea, or circadian rhythm sleep-wake disorders (Ohayon, 2011; Petit et al., 2007).

Parasomnias are related to abnormal experiences coinciding with sleep such as sleepwalking (Ohayon, 2011; Petit et al., 2007). Furthermore, sleep disorders have been associated with significant impairment to health-related quality of life (Darchia et al., 2018). A meta-analysis by van Straten et al. (2025), estimates that approximately 12.4% of the global population is diagnosed with insomnia. The diagnostic criteria for being diagnosed with insomnia includes difficulties initiating or maintaining sleep at least three days a week for a period greater than three months that is not otherwise explained situationally or by existing physical and mental illness including substance use (American Psychiatric Association (APA), 2013; van Straten et al., 2025). A diagnosis of insomnia is further characterised by having a significant impact on the individual's wellbeing (APA, 2013; van Straten et al., 2025). Pooled findings from a systematic review and meta-analysis by Blaszczyk et al. (2023) suggests a 16% prevalence of primary migraine in participants with obstructive sleep apnoea. Migraine and sleep apnoea comorbidity may be partially explained by shared comorbidities such as obesity (Tiseo et al., 2020). Sleep apnoea may further be a causal factor for migraine and is considered under headache related to disorder of homeostasis (IHS, 2018). If migraine and OSA diagnoses coincide

temporally, the distinction between secondary migraine and primary migraine in individuals with OSA can be made considering the nature of headaches. Headaches which reoccur in the morning after sleep that also resolve with nasal continuous positive airway pressure therapy, the primary approach to treatment in OSA, indicates secondary causation (Goksan et al., 2009; IHS, 2018).

1.4. Sleep and Circadian Rhythms in Migraine

1.4.1. Subjective Sleep in Migraine

The interaction and relationship between sleep and migraine is bidirectional, whereby sleep may impact migraine, and migraine may impact sleep (Ikram, 2025; Korabelnikova et al., 2020; Ouyang et al., 2024; Thomaz et al., 2021; Vygontzas & Pavlovic, 2018). Migraine symptoms such as phonophobia and nausea have further been found to impair sleep quality as measured by the Pittsburgh Sleep Quality Index. A study by Schumacher et al. (2023) found that global PSQI scores were significantly associated with migraine frequency and phonophobia. Sub scores of sleep efficiency were further significantly related to migraine frequency, medium frequency nausea and phonophobia. This may be partially because of phonophobia making individuals more sensitive to sound and further disrupting sleep quality and poor sleep efficiency making migraine occurrence, and phonophobia more likely (Schumacher et al., 2023).

The relationship between sleep and migraine seems to begin in the early stages of the condition with sleep disturbances occurring more frequently in children with migraine than healthy children. A study by Miller et al. (2003) observed a significant predictive relationship between migraine frequency and duration with sleep disturbances as measured by the Children's Sleep Habits Questionnaire such as

delayed sleep onset, bedtime resistance, sleep duration, daytime sleepiness, night wakings, sleep anxiety, parasomnias and sleep disordered breathing. Such results were also found in systematic review by Tiseo et al. (2020) which highlighted the comorbidity of migraine among adults with sleep disorders including insomnia (25.9%), sleep related breathing disorder (13.7% to 25%), parasomnias such as REM sleep behaviour disorder (24.2%) and somnambulism (33%), hypersomnolence such as narcolepsy (23.5% and 37%) and idiopathic hypersomnia (41.2%) and sleep related movement disorders such as restless leg syndrome (12.6% to 53.2%). Like much of the research on migraine, the reliability of the results obtained by Miller et al. (2003) are questioned by opposing findings. An actigraphy study in children with migraine found that between attacks, there were no significant differences in sleep duration, sleep efficiency, index of motor activity and wake after sleep onset (Bruni et al., 2004). Sleep latency however was significantly different with the paediatric migraine group taking longer to fall asleep than nonmigraine controls (Bruni et al., 2004). No significant differences in these variables were observed within the migraine group, across stages of an attack apart from index of motor activity which was significantly lower during the prodromal stage before an attack compared to between, during and following attacks (Bruni et al., 2004). While some differences were observed, these objective findings do not highlight the same level of impairment of the subjective reports observed by Miller et al. (2003).

Too much sleep too has often been reported by migraine sufferers to be an aggravating factor or trigger for attack onset. The pathophysiological mechanisms behind this are unclear. A study by Vgontzas et al. (2021) found that in a longitudinal prospective cohort study with 97 adults with episodic migraine that over 80% of migraineurs napped during the study particularly during the headache phase

compared to between attacks. In this study, napping was associated with an increased number of headache days per month and was not associated with subjective or objective sleep quality (Vgontzas et al. 2021). A study by Ong et al. (2023) examined the relationship between migraine and sleep behaviours including naps and nighttime sleep using a mixed design. Frequency and duration of naps was examined between migraineurs and age and sex-matched controls while within groups, mixed models investigated the temporal relationship between headache characteristics (pain severity), parameters of sleep behaviours (nap frequency, nap duration) and nighttime sleep efficacy (Ong et al., 2023). Results from this study found that during the 4-week period of the study, migraineurs reported significantly more naps compared to controls. Furthermore, a significant association was observed between increased migraine severity and longer nap duration. Nap duration was then in turn associated with lower sleep efficacy, while greater sleep efficacy was associated with earlier sleep onset, longer time in bed and later sleep end (Ong et al., 2023). Migraineurs further displayed significantly more symptoms of insomnia as measured by the Insomnia Severity Index as well as 65% of the migraine group meeting the Pittsburgh Sleep Quality Index cut-off for poor sleep. Such was not observed among any of the control participants. Self-reported fatigue was also significantly greater in the migraine group (Ong et al., 2023). A meta-analysis from Stanyer et al. (2021) observed significant differences in scores on the Pittsburgh Sleep Quality Index with migraineurs having higher scores, indicating poorer sleep quality compared to healthy controls. Furthermore, sleep quality varied within groups with poorer sleep quality among chronic migraineurs than those with episodic migraine (Stanyer et al., 2021).

Similar findings of impaired sleep effects have been observed using the Karolinska Sleep Questionnaire which assesses subjective sleep and sleepiness (Nordin et al., 2013). A study by Ødegaard et al. (2010) observed that participants with migraine displayed significantly higher scores than participants with no migraine. Furthermore, 33.3% of migraineurs displayed severe sleep disturbances measured by upper quartile scores of the KSQ (Ødegaard et al., 2010). Following adjusting for the covariates of age, sex, and sleep medication, the odds for severe sleep disturbances were 5 times more likely for migraineurs compared to non-migraine controls (Ødegaard et al., 2010). Migraine frequency further implicated sleep with chronic migraineurs being nearly 39 times more likely to score in the upper quartile of the KSQ, and 30 times more likely following adjustment for affective scores of anxiety, and depression (Ødegaard et al., 2010).

Further research by Duan et al (2022) found that poor sleep quality significantly increased the likelihood of migraine occurrence. In this study, multivariate logistic regression revealed that 1 standard deviation increase in PSQI scores made migraine occurrence 1.6 times more likely. In a subgroup of participants with poor sleep quality, migraine was nearly 4 times more likely to occur. Poor sleep quality was further found to increase pain severity and burden, mood impairment (anxiety and depression), and poorer quality of life in participants with migraine. Further supporting the importance of sleep in the condition, a study by Bag et al., (2023) further observed a significant moderate association between headache frequency and sleep quality measured using the Pittsburgh Sleep Quality Index. Poor sleep quality was further observed to be significantly associated with migraine frequency in individuals with and without aura (Lin et al., 2016). The relationship between migraine and sleep quality over time may vary among female migraineurs,

particularly as the female reproductive system changes during the stages of menopause. A study by Faubion et al. (2024) found that migraine history significantly predicted poor sleep (PSQI >5) in pre and peri menopausal women; however, after accounting for covariate anxiety and depression, this relationship was only observed in premenopausal women. These findings suggest a greater role for anxiety and menopausal symptoms in sleep impairment during the later stages of menopause rather than migraine diagnosis (Faubion et al. 2024).

A narrative review by Yang and Wang (2017) suggests that the role of sleep behaviours in migraine may lower the threshold for migraine onset and as such lead to greater risk for migraine and maladaptive coping behaviours to deal with sleep disturbances and migraine pain, reinstating the vicious cycle. Sleep disorders are furthermore prevalent among migraineurs in comparison to the general population. A study by Kim et al. (2018) found that the prevalence of migraine in participants with insomnia was nearly three times greater compared to participants without insomnia. A review by Tiseo et al. (2020) suggests a bidirectional relationship between insomnia and migraine with a diagnosis of either condition making it significantly more likely to develop the other. Alongside this, there is a bidirectional relationship between the conditions, whereby the effects of each may worsen the other. For example, migraineurs suffering from insomnia report more severe migraine pain and increased attack frequency which may be explained by worsened habituation to painful stimuli and changes in pain processing because of sleep impairment (Simpson et al., 2018; Tiseo et al., 2020). Similarly, night-time migraine pain may disturb or fully prevent sleep highlighting the potential cyclical worsening of both sleep and migraine. The relationship between insomnia and migraine is independent from anxiety and depression (Tiseo et al., 2020).

1.4.2. Objective Sleep in Migraine

A study by Daghlal et al. (2020) using the UK biobank and International Headache Genetics data sets observed significant genetic correlations between migraine and sleep traits such as symptoms of insomnia, difficulty awakening, sleep duration, napping and daytime sleepiness. Results from this study further observed increased risk for migraine in individuals with difficulty waking up and increased likelihood of insomnia (Daghlal et al. 2020). Using a cross-sectional, Bayesian approach, a study by Stanyer et al. (2023) examined the relationship between sleep and migraine in a global sample collected from a mobile application. In this study, sleep start and end times, migraine onset and pain intensity were recorded from a sample of 11,116 global users. Of the measurements included sleep disruptions and deviations from mean sleep duration significantly predicted next day migraine onset. No significant predictive effect of total sleep duration was observed on next day migraine onset. This may further suggest a significant role of sleep regularity in migraine and may underpin circadian components of the disorder. Not surprisingly, results indicated pain intensity was significant predictor of sleep duration in the sample (Stanyer et al. 2023). Sleep and circadian functioning may play an incrementally significant role as migraineurs age. A study by Gori et al. (2012) found that the frequency of attacks occurring during the night when sleeping and at wakening gradually increased in each of the age groups (20-30 years; 31-40 years; 41-50 years; 51-60 years and 61-70 years) with 58% of migraineurs between 61- and 70-years experiencing sleep related migraine. Gori et al. (2012) suggest this may be a result of degeneration of the suprachiasmatic nucleus with age which implicates the release of melatonin. Research by Göder et al. (2001) used polysomnography in individuals with migraine across nights that were and were not preceding a migraine attack. The results from this study observed decreased rapid eye movement density,

decreased beta power in N3, and decrease alpha power during the first R period in the nights preceding a migraine attack (Göder et al., 2001). Göder et al. (2001) suggest that the decrease in alpha power during the R period may be interpreted as an increased need for sleep prior to migraine onset as previous research has shown this effect with reduced sleep duration in the previous nights (Merica et al., 1998, as cited in Göder et al., 2001). Göder et al. (2001) further suggest that the decrease in beta power in slow wave sleep may be due to the decrease in nervous system activity prior to migraine. A meta-analysis by Stanyer et al., (2021) further observed similar findings of reduced REM sleep in individuals with migraine. Stanyer et al. (2021), discusses the implications of reduced REM sleep in worsening migraine symptoms such as cutaneous allodynia, however, the role of REM sleep in migraine is yet to be fully understood.

1.4.3. The Chronobiology of Tension Type and Cluster Headaches

Little research exists on the chronobiology of tension-type headache. In a study by Im et al. (2019) 44.8% of individuals with tension-type headache reported a time preference for headache attack. However, no significant difference in chronotype was observed between those with or without time preference of attack (Im et al., 2019). Similarly, no significant association was observed between headache frequency and chronotype (Im et al., 2019). Unlike tension-type headache, research on cluster headache depicts a significant circadian profile to the disorder. Research suggests seasonal changes from winter to spring and autumn to winter associated with change in temperature increased the risk of attacks however meta-analysis reveals October to be the peak month for headache occurrence (Benkli et al., 2023; Lee et al., 2014). Daily time preference has also been recorded in research suggesting that attacks peaked nocturnally at 2am and least likely to occur at specific

times during the day (8-9am, 11am-12pm and 5-6pm) (Barloese et al., 2015; Rozen & Fishman, 2011). However, some research suggests that the rhythmicity of attacks may fluctuate across time (Lee et al., 2018). Furthermore, a genetic analysis by Benkli et al. (2023) highlights some genes linked to cluster headache (UFL1, MERTK and SATB2) displayed circadian cycling and may help to explain the rhythmicity of cluster headache.

1.4.4. The Chronobiology of Migraine

The role of “the hypothalamus and the orexigenic system in pain modulation, feeding, arousal and sleep regulation... provide a causal link between the possible origin for the triggering” of migraine headache (Goadsby et al, 2017 p.572). The hypothalamus is central to maintaining homeostasis by regulating autonomic, endocrine and circadian processes, among numerous other physiological processes, many of which are also implicated in migraine (Goadsby et al., 2017). Salinas-Abarca et al. (2025) highlight numerous hypothalamic neurotransmitters which are implicated in migraine including orexins, neuropeptide Y, pituitary adenylate cyclase-activating peptide (PACAP), oxytocin, and vasopressin. The regulation of physiology and behaviour by the hypothalamus is due to the body’s biological clock; circadian rhythms which synchronise physiological and behavioural processes with environmental rhythms during the 24-hour day (Roenneberg et al, 2019; Roenneberg & Merrow, 2016; Singh, 2009). The overlap of the hypothalamus in headache and circadian rhythms, highlight the potential of chronobiological approaches to understanding and treating headache. A study by Zele et al. (2021) observed that in comparison to healthy controls, migraineurs displayed significantly greater and longer melanopsin activity via the post-illumination pupil response. In this study, migraineurs also displayed reduced pupil constriction within the two-day period

following an attack. Light is further intrinsically linked to migraine as a commonly reported headache trigger but also as a symptom of the condition being photophobia, worsening pain in response to light and avoidance of light. The pathophysiological role of light in migraine onset is unclear however findings from Nosedá et al. (2015) found that the ganglion cells of the retina had axons linking to hypothalamic neurons which projected to the nuclei of brainstem and spinal cord which are involved in sympathetic and parasympathetic functions in rats. Neurotransmitters found in this network include dopamine, histamine, orexin, melanin-concentrating hormone, oxytocin, and vasopressin (Nosedá et al., 2015). The authors of this paper however suggest that this conceptualisation of the potential mechanisms underlying migraine onset may be simplified in comparison to human migraine patients (Nosedá et al., 2015).

An experimental study by Fathy, AbdAllah and Helal (2023) tested serum melatonin levels between migraineurs and healthy controls using morning and evening blood samples. Results from this study found significantly lower melatonin levels in migraine patients in both morning and evening serum samples (Fathy, AbdAllah & Helal, 2023). Correlation analysis observed a significant, negative association between melatonin levels, attack frequency, sleep quality, and level of disability in the migraine group (Fathy, AbdAllah & Helal, 2023). Further examination found that serum level melatonin was significantly lower in migraineurs with aura than those without and chronic migraineurs (Fathy, AbdAllah & Helal, 2023). Research from Ong et al. (2018) found that there were no differences in sleep actigraphy or circadian phase measured by salivary melatonin between chronic migraineurs and controls. However, within the chronic migraineurs increased headache frequency was significantly associated with delayed onset melatonin and

later midpoint of sleep. Using internal circadian phase and sleep midpoint, Ong et al. (2018) calculated phase angle and found that greater phase angle was associated with increased migraine disability.

While many questions remain in headache research, the importance of sleep as an aggravating factor in primary headache has been documented in the literature (Freedom & Evans, 2013; Van Oosterhout et al, 2018). Recent research in chronobiology has observed circadian relationships in the understanding of primary headache and its neurological mechanisms (Burish et al, 2019; Fox & Davis, 1998; Freedom & Evans, 2013; Sullivan & Martin, 2017; Van Oosterhout et al, 2018). Research has found that early chronotypes experience migraine significantly more than late chronotypes; with late chronotype predicting chronic non-migraine headache (Sullivan & Martin, 2017; Van Oosterhout et al, 2018). Furthermore, research has found temporal preference of migraine onset with most occurring early morning; congruent with chronotype (Fox & Davis, 1998).

Research suggests that more extreme chronotypes overall are more likely to experience migraines which may be due to circadian rigidity and sensitivity to changes or disruption of circadian rhythms (Van Oosterhout et al, 2018). Poor sleep quality has been observed in both migraine and tension-type headache although its prevalence is much higher in migraine populations (Gori et al, 2005; Sullivan & Martin, 2017). Late chronotypes typically experiences more sleep deprivation than early types due to later sleep onset conflicting with the demands of the social world (i.e. work, school) which can precipitate headache (Roenneberg et al, 2019). Little research has investigated chronotype differences in headache severity and those which have, report no significant results (Viticchi et al, 2019). However, headache severity has been shown to be impacted by sleep quality; with poor sleep quality

increasing sensitivity to painful stimuli and worsening tolerance to headache (Alexandre, 2017; Benito-González et al, 2018; Ferini-Strambi, 2017; Lee et al, 2013; Ong et al, 2018).

The relationship between circadian rhythms and migraine is complicated and its understanding is made difficult by limited research into the topic. A review of clinical studies by Baksa et al. (2019), examined 10 studies meeting the search criteria of “migraine” and circadian”. Results from this review observed varying results with some studies reporting monophasic and biphasic 24-hour cycle to migraine onset (Baksa et al. 2019). Furthermore, lack of control over various confounding variables of medication, secondary conditions, abnormal work hours and sample size made synthesising results difficult (Baksa et al. 2019). Mechanisms suggested by these studies included hypothalamic dysfunction, circadian variation of triggers, morning rhythmic cortisol increase, and abnormal circadian rhythms (Baksa et al. 2019). Some research exists which suggests rhythmicity of migraine attack onset, A review by Poulsen et al. (2021) suggests that migraine attacks are more frequent in the morning between 6 am and 12pm. Poulsen et al. (2021) further suggest migraine attacks are more frequent on the weekends, particularly Saturday. Research however, such as that by Van Oosterhout (2017) which is included in the review by Poulsen et al. (2017) suggests that timing on migraine attacks may be related to individual chronotype. Further, metabolic understandings of migraine such as that by Gross et al. (2019), leave potential for the role of dietary factors which overlap with chronobiology in migraine pathophysiology (Cavestro, 2025; Grech et al., 2022). However, this link is hypothetical and not yet examined in research.

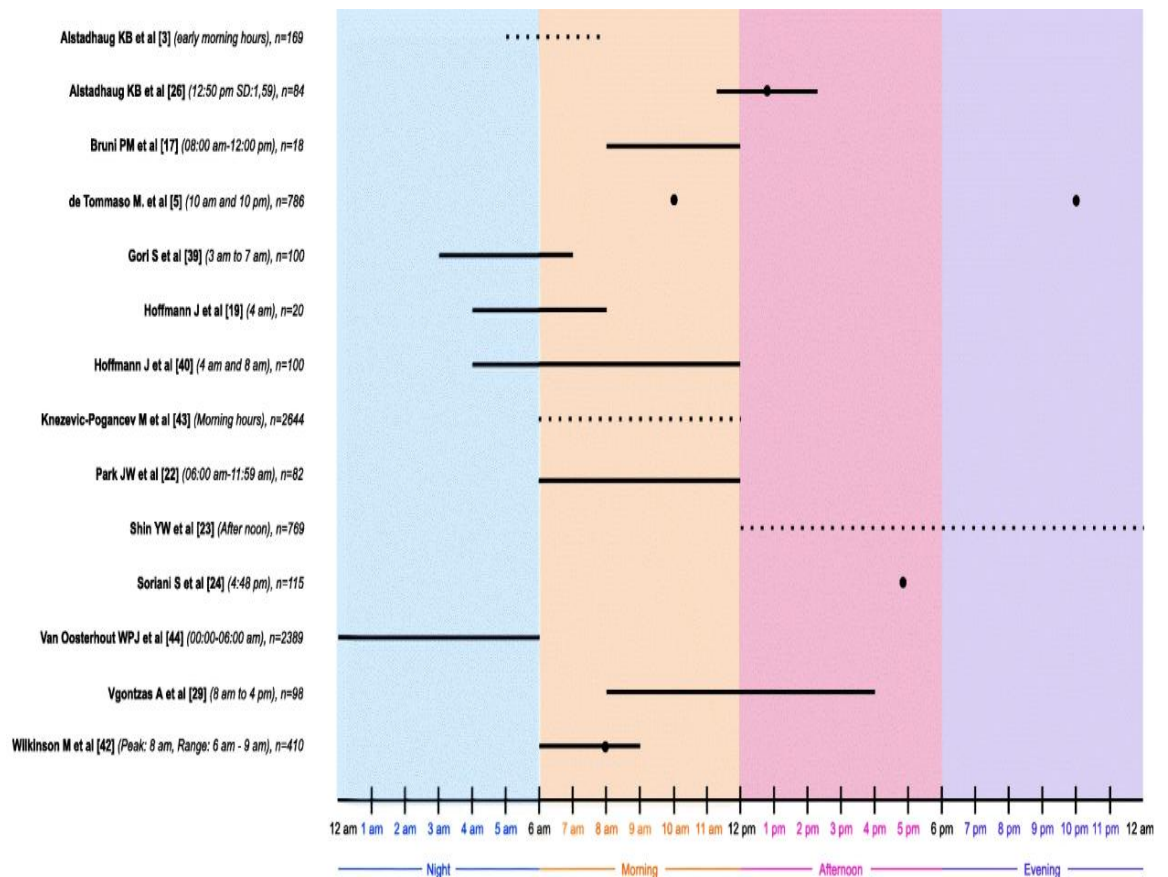


Figure 1. 2. Figure taken from Poulsen et al. (2021), which highlights the clock time (x axis) distribution of migraine attack onset across 15 studies (y axis) included in the review. Dotted lines in the figure represent estimated times based on categorical time points used in three of the studies. Black dots represent exact time reports in two of the included studies. Greatest overlap in migraine time onset was observed between 6 am and 12pm.

1.4.5. Routine in Migraine

With research highlighting a circadian component to migraine and the activation of the hypothalamus during the prodrome or potentially prior to migraine, a more thorough examination of the role of homeostatic balance and routine is warranted. A review by Seng et al. (2022) which examined lifestyle behaviours and migraine suggest that unusual disruptions to daily routine were typically associated

with the onset of a migraine attack. In this review, it is also suggested that increases and decreases in stress may trigger the onset of an attack. Bidirectional implications of sleep have been demonstrated in research with too much or too little sleep triggering an attack (Sullivan & Martin, 2017). Sleep quality is another factor known to impact migraine with poor sleep, marked by disturbances and less restoration further initiating attacks (Seng et al. 2022). Seng et al. (2022) also suggest changes in diet to be important as previously discussed. Furthermore, fasting and skipping meals as well as overeating has been shown to trigger migraine attacks (Kelman, 2007). The role of missed meals or fasting on migraine onset has been argued to be due to hypoglycaemia (Legesse et al., 2025).

The effect of maintaining a continuous healthy lifestyle may be more significant to chronic migraine rather than those with frequent or infrequent migraine. A study by Woldeamanuel and Cowan (2016) examined the variables sleep, exercise and mealtimes on the likelihood of having chronic migraine and found that maintaining regular lifestyle behaviours acted as a protective factor between episodic and chronic migraineurs. This study further found that having regular sleep, exercise and mealtimes were associated with better outcomes than mealtimes and exercise, suggesting that of the three, regular sleep is the most crucial factor in preventing migraine progression.

Furthermore, research on exercise on migraine has highlighted that while regular exercise can act as a protective factor, in individuals who do not exercise regularly, it has been reported to be a trigger factor. It is suggested that individuals with migraine who exercise more frequently build a higher threshold in response to the exercise effects on peptide levels such as CGRP and metabolism (Amin et al., 2018).

1.4.6 Dietary Factors in Migraine

Various migraine triggers are reported to involve food and eating behaviours and the nature of these behaviours in being aggravating factors for migraine is not clear. A study by Amani Tirani et al. (2023), suggests that a good quality diet may be important in the manifestation of migraine. Results from Amani Tirani et al. (2023), found that greater variation or diversity in diet was significantly associated with lower migraine frequency. No association however was observed with migraine severity, impact, or duration. Irregular eating patterns such as fasting and hunger is another commonly reported migraine trigger (Dalkara & Kiliç, 2013). Research by Ragab et al. (2021) with individuals fasting during Ramadan found that the frequency of migraine attacks was significantly greater during Ramadan compared to the month prior. Furthermore, attack frequency and pain intensity was significantly greater in the first ten days of Ramadan compared to the second and third ten-day periods following (Ragab et al., 2021). Descriptive analysis further revealed for the majority of migraineurs, migraine onset began during the fasting period of the day (77.8%) (Ragab et al., 2021). Similar findings were observed in Mustelin et al. (2014) which found that individuals with an eating disorder such as anorexia nervosa and bulimia nervosa had a significantly higher risk of having migraine and major depressive disorder. However, stepwise regression examining migraine with disordered eating accounting for major depressive disorder as a covariate, found no significant association, suggesting the mediative role of depression on disordered eating observed in the migraine group (Mustelin et al., 2014). Further research by Demirci et al. (2015) examining attitudes to eating has found that using Eating Attitudes Test, migraineurs scored significantly higher scores than healthy controls suggesting disordered eating. Further correlational analysis observed significant,

positive associations between eating attitudes and depression with migraine disability in the migraine group (Demirci et al. 2015). Eating attitudes were also separately and significantly associated with levels of anxiety and depression in both groups (Demirci et al. 2015).

Research has found that late chronotypes are more impulsive than early chronotypes and consume more stimulants such as nicotine, alcohol and caffeine which are documented aggravating factors for headache (Fabbian et al, 2016; Roenneberg et al, 2019; Wittmann et al, 2006). Habitual caffeine use has been observed to increase the hyperexcitability of brain cortices and cause primary headache (Alstadhaug & Andreou, 2019; & Espinosa Jovel & Sobrino Mejía, 2017; Shapiro, 2008). Alcohol has further been self-reported by migraineurs as a trigger for migraine onset however, more research is needed to understand the chemical properties which make specific alcohols trigger headache (Davis-Martin et al, 2017; Dueland, 2015; Onderwater et al, 2018; Panconesi, 2016; 2008). Research suggests that more frequent or habitual alcohol use, which varies with culture, could mediate the role of alcohol as a trigger in primary headaches (Panconesi et al, 2013). The role of nicotine as a headache trigger is unclear; however, research has found habitual smokers to have greater headache prevalence (Aamodt et al, 2006; Millea & Brodie, 2002).

Further variation in dietary behaviours has been observed between chronotypes. Late types on average consume more unhealthy food and have overall poorer diets than early types which further may influence interaction with dietary triggers and headache onset (Arora & Taheri, 2015; Partonen, 2015). Research has indicated that the role of dietary triggers that precipitate headache may be due to hypothalamic regulation of behaviour via circadian rhythms (Alstadhaug & Andreou,

2019; Arora & Taheri, 2015; Davis-Martin et al, 2017; Onderwater et al, 2018).

Research has found that consuming unhealthy foods such as those with monosodium glutamate, nitrates, and aspartame, which are found in many processed and unhealthy food items may act to trigger headache (Martin & Vij, 2016a).

Furthermore, Martin & Vij (2016b) suggest healthier low-fat diets, diets with high folate or omega-3 may help in preventing primary headache by aiding the regulation of vascular tone (Ferrara et al, 2015; Razeghi-Jahromi et al, 2019).

More recent research has investigated the role of dietary parameters on migraine characteristics (Bakirhan, Yildiran and Uyar Cankay, 2023). Interestingly, results from this study found numerous significant associations of migraine characteristics (as measured by MIDAS) with body composition and nutritional intake. Positive correlations were observed between migraine severity, muscle mass percentage, cholesterol, serum thyroxine, energy, and carbohydrate intake. A negative correlation was observed between monounsaturated fatty acid, fibre, vitamin C and migraine severity. Muscle mass percentage was negatively correlated with attack duration. Higher bone mass was associated with reduced migraine frequency whereas protein and vitamin B2 intake were associated with increased attack frequency. High body fat percentage and cholesterol level were associated with increased attack duration (Bakirhan, Yildiran & Uyar Cankay, 2023).

Adherence to healthy diet patterns as measured by the alternative Healthy Diet Index (HDI) was observed to reduce the duration of migraine by 43% in comparison to participants with poor adherence to the HDI (Khalili et al., 2023). Healthy diets which are less reliant on saturated fats and processed foods have further been found to improve wellbeing in migraine patients with significantly lower odds of having migraine in comparison to a more westernised diet marked by

high saturated fat, sugar, and processed foods (Martami et al., 2023). Migraine frequency varied significantly across consistency of diet with participants who scored higher scores on the western diet having a significantly higher frequency of attacks than those with lower adherence to the western diet (Martami et al., 2023). The relationship with diet and lifestyle in migraine is further explored by research examining the relationship between migraine and obesity. A study by Fan et al. (2024), found that extended migraine pain or duration of pain was significantly associated with increased weight, waist circumference, body mass index, and body fat percentage. Research by Caprio et al. (2023) has further found that adherence to a low-calorie ketogenic diet is effective at reducing the number of migraine days experienced each month in comparison to a low-calorie balanced diet. These findings contrast those of Bakirhan, Yildiran and Cankay (2023), as a defining feature of a ketogenic diet is that of high intake of protein and fats which were shown to worsen migraine frequency and severity. The role of diet and metabolism is strengthened by studies such as Amendolara et al. (2024), who found that all three male migraineurs in the case series displayed hypoglycaemia three hours after eating. After following a three-month ketogenic diet, all three participants experienced a reduction in migraine frequency. However, glucose tolerance was not tested again during this period so no comparison can be made. These findings although not inferential of the general population strongly suggest a role for metabolic disturbance in migraine.

1.5 Cognitive and Psychosocial Impacts of Migraine

1.5.1. Cognition in Migraine

One frequently reported and overlooked consequence of migraine is the impact of migraine on cognitive function. Cognitive symptoms such as difficulty

concentrating, language impairments and brain fog are frequently reported by individuals with migraine as occurring in all stages of the migraine attack, during the prodrome, the headache and the postdrome (Gil-Gouveia & Martins, 2018). Various research has suggested cognitive changes at a biological level. For example, a review by David et al. (2020) found that neuroimaging revealed increased activation and abnormal functioning of cortical areas intrinsic to memory processing and formation, the integration of sensory information and temporal cortical areas responsible for language and visuospatial functioning (see also Ravishankar & Demakis, 2007). Similarly, a systematic review found abnormal functional connectivity in various networks, including “salience, sensorimotor, executive, attention, limbic and default mode networks, and networks related to visual processing” (Chong et al., 2019: p6). A review by Liu et al. (2018) further suggests abnormal functional connectivity of the hippocampus at resting state in migraineurs. However, translations into cognitive assessments have been less convincing with some research finding no significant impairments in migraine populations (De Araujo et al., 2012; Vuralli et al., 2018). Whereas other studies have suggested that even between attacks, migraineurs displayed impaired cognitive functioning compared to healthy controls (Braganza et al., 2022). As such, there are conflicting results on the cognitive profile for migraine. The sporadic nature of migraine further implicates cognitive research, as cognitive symptoms are reported in the days preceding and following an attack, it is possible that research fails to capture transient impairment.

1.5.2. Mood in Migraine

The high prevalence of mood disorders and impairment is widely recognised in the literature. A national population-based study by Jette et al. (2008) observed that individuals diagnosed with migraine were more than twice as likely to have

major depressive disorder and bipolar disorder. Furthermore, participants with both migraine and a psychiatric disorder suffered poorer outcomes such as reduced quality of life, greater functional impairment and greater use of mental health services. Comparable results were observed in a prior population-based study by Molgat et al. (2005) which found that the prevalence of major depression disorder in Canadian migraineurs was just over twice that of healthy individuals. However, this study also included data from individuals with chronic conditions other than migraine and found that prevalence of major depression disorder (MDD) in this group was comparable to that of healthy individuals. Similarly, individuals diagnosed with mood disorders have a greater risk for developing migraine; highlighting the bidirectional relationship of the two disorders (Marino et al., 2010). This further suggests that the relationship between migraine and disordered mood is that of a shared pathology rather than the experience of living with migraine. The link between migraine and mood disorder is the serotonergic system and subsequent serotonin (5-HT) levels between and during attacks. Sicuteri et al., (1961) initially observed increased urinary serotonin in migraineurs during the attack in comparison to controls. The level of excreted urinary 5-hydroxyindoleacetic acid (5-HIAA, a metabolite of serotonin) varied among the migraineurs, with some migraineurs excreting significantly higher levels, over two times that of controls, to no significant differences between the groups. However, a review by Hamel (2007) has summarised research on serotonin the neurotransmitter and its metabolites, which have shown increased plasma 5-HT levels and reduced urinary 5-HIAA levels during the attack and the opposite interictally; low plasma 5-HT and high urinary 5-HIAA (Ferrari et al., 1989; Humphrey, 1991; Ferrari & Saxena, 1993; in Hamel, 2007). These findings, suggest an implicated serotonergic system, which results in low baseline serotonin levels whereby an increase initiates the migraine onset

(Hamel, 2007). In the same regard, further studies on the role of serotonin in people with depression have found reduced serotonin receptors and reduced serotonin receptor binding in multiple areas of the cortex (Wang et al., 2016). This is supported by more recent studies which have further found a significant overlap in genetic factors for migraine and MDD (Androulakis et al. 2023). The use of selective serotonin reuptake inhibitors in treating mood disorders such as depression further emphasises the overlap in the underlying neurobiology of both migraine and depressive disorders (Marino et al., 2010). However, the role of serotonin in depressive disorders has been debated, as not all studies have found convincing or consistent results and long-term use of anti-depressant medication may reduce serotonin concentration (Moncrieff et al., 2023). Other reviews suggest that rather than a chemical imbalance theory, the role of serotonin implicates cognitive functioning such as the appraisal of rewards, which alongside other processes, may lead to depressive symptoms and behaviours (Jauhar et al., 2023).

1.5.3 The Impact of Pain on Cognition

The bidirectional relationship between pain and cognition is well documented in the literature (Gong et al., 2025). Pain is not merely a sensory experience but rather involves affective and cognitive-evaluative dimensions (Melzack & Casey, 1968; Moriarty et al., 2011). It is conceptualised that the experience of pain involves a number of cognitive processes including attention, emotional regulation, executive functions (decision making, working memory, expectations of pain) and long-term memory (the meaning of pain and prior experience of pain) (Eccleston, 1994; Legrain et al., 2011; Ploghaus et al., 2000; Wiech et al., 2008). As such, there is significant overlap between pain and cognition, with pain perception and modulation relying on cognitive processes. Pain has been found to impact cognitive

test performance (Moore et al., 2012). For example, in instances of acute pain, deficits in attention have been explained in terms of pain acting as a competing demand which impacts performance on tasks that require attentional control (Eccleston, 1994; Moore et al., 2012).

However, unlike acute pain, chronic pain has significant physiological effects as individuals with chronic pain conditions display implicated neural plasticity, neuroinflammation, neurotransmitter levels alongside structural and functional neural changes (Gong et al., 2025). For example, one study observed that individuals with chronic pain display maladaptive neuroplasticity changes in the prefrontal cortex, insula and basal ganglia alongside reduced prefrontal gray matter (Shiers & Price, 2020). Pain medications which relieve pain are further ineffective at preventing cognitive impairment and physiological changes to the brain (Gong et al., 2025; Schiltenswolf et al., 2014). Interestingly, gray matter volume has proven to be restorable through cognitive behavioural therapy and preventative pain management, supporting the role of neuroplasticity rather than neurodegeneration (Shiers & Price, 2020). Long-term impacts on physiology are less understood, however, as research has observed chronic pain to be a significant predictor of cognitive decline and dementia in older adults (Yuan et al., 2023).

In terms of the neuropsychological impact of chronic pain, research has observed deficits in general measures of cognition such as Mini-Mental State Exam and Cognitive Capacity Screening Exam, as well as domains of attention, learning and memory (spatial, verbal, recognition, and long-term memory), reaction time, psychomotor ability and controlled executive functions such as task switching (Gong et al., 2025; Moriarty et al., 2011). Although chronic migraine is classified as a neurological disorder, it is further recognised as a chronic pain condition,

highlighting the complexity of examining cognitive function in migraine and determining what impairment is migraine-specific and what impairment is a result of reoccurring pain (Fernandes et al., 2024).

1.5.4. Psychosocial Impact of Migraine

The impact of migraine goes beyond the individual and is often observed in the social context, impacting on their engagement in society, ability to work or learn and their relationships with others. Leonardi and Raggi (2019) suggest that the impact of migraine is not always tangible and may impact on everyday life. In their review, Leonardi and Raggi (2019) suggest that individuals with migraine lost on average 10.2 work-equivalent days measured using days absent from work and presenteeism; where individuals attended work but were significantly impaired and less productive. However, this varied among studies, with productivity loss ranging from 3.2 to 89.2 work equivalent days per year (Leonardi & Raggi, 2019). Migraine is associated with a significant socioeconomic burden, with a German population-based study estimating that the monetary loss consequential to migraine is €100.4 billion per annum (Seddik et al., 2020). Socioeconomic cost in this study, however, was calculated by taking in to account the sum of paid and unpaid work, the cost associated with service and medication use and induced effects as a consequence; for example: reduced spending, less engagement with services and further ripple effects caused by the initial, direct employment cost (Seddik et al., 2020). Substantial economic costs have been estimated in a UK study that estimates a cost of £130.63 per migraine episode, equating to £12.2 billion annually with predicted social productivity costs of £5.81 billion (Martins et al., 2023). Migraineurs are not only absent from work but often are unable to attend social and leisure activities. A study by Awaki et al. (2024) demonstrated that on average, individuals with migraine

missed social events with friends and family 1.4 days (SD = 4.5) in the previous three months. The same study further found migraine prevented participants from engaging in activities of daily living such as driving and exercising (Awaki et al., 2024). Similarly, over half of the participants in the study reported needing help in day-to-day activities in and outside of the home at least a little bit of the time (Awaki et al., 2024). Furthermore, the psychosocial impact of migraine further goes beyond the attack and the wide array of symptoms. The interictal burden of migraine as a sporadic condition is another aspect that is often less considered; that even between attacks, migraine impacts daily living (Hubig et al., 2022). Many individuals with migraine attempt to self-manage their condition through regulating their behaviour to reduce exposure to perceived migraine triggers such as exercise, specific foods or more general sensory stimuli like as loud music and strong smells (Lo et al., 2022).

The inability to engage fully socially is further emphasised by research which has shown that nearly half of all migraineurs in a sample were classified as lonely, which was also significantly more likely in individuals with chronic migraine compared to individuals with episodic migraine (Lui et al., 2020). The impact of migraine is further observed in close relationships where it can be a source of stress and strain (Buse et al., 2016). Research on the impact of migraine on spouses and children of individuals with migraine has found that migraine impacts on intimacy and the division of labour in the home, with children of single parent migraineurs missing school and having to help around the home (Ruiz de Velasco, 2003). As such migraine partners have expressed a lack of satisfaction with their partners ability and the increased responsibility put on them at home and work to compensate for the disability caused by their partners migraine (Lipton et al., 2003). While partners of migraineurs were more understanding of the impact and severity of

migraine than individuals with migraine believed, various research has highlighted that family and friends maybe less understanding or aware of the level of disability and impairment caused by migraine (Buse et al., 2016; Pirthiraj & Bhagwan, 2023). However, the perceived lack of understanding by others may represent internalised stigma where migraineurs have absorbed negative understandings of their condition (Casas-Limón et al., 2024).

Stigmatisation of migraine is prevalent in every aspect of the social sphere, it is demonstrated in social groups, the workplace and even at a structural level where migraine research is underfunded and under-recognised as a legitimate disability or illness (Casas-Limón et al., 2024; Parikh & Young, 2019). Part of the lack of understanding around migraine is due to the “invisible” nature of the condition and the common misunderstanding that it is just a headache, without acknowledging the severity of the pain or the full range of symptoms that co-occur (Battista et al., 2023). A study by Goodhew (2019) found that migraine literacy was incomplete in individuals with and without migraine. In this study, 31% of non-migraineurs believed that migraines have the same symptoms as other headaches and 35% believed that there were no sensory disturbances in migraine (Goodhew, 2019). Most concerning, only 38% of non-migraineurs reported correctly that migraine episodes typically lasts hours to several days and only 42% correctly reported that migraine headache was aggravated by routine physical activity (Goodhew, 2019). Furthermore, increasing migraine literacy in the general public may help to reduce public, structural and internalised stigma (Casas-Limón et al., 2024). Internalised stigma in individuals with migraine has significant consequences for mental wellbeing through negative feelings of guilt, frustration and shame due to the impact

of migraine on the individual's inability to meet normative expectations of functioning (Estave et al., 2021; Palacios-Ceña et al., 2017).

1.6 Migraine Treatment

1.6.1 Medication

Much of the literature and direction of migraine care has been focused on pharmacological interventions (Alsakhairi et al., 2024). Pharmacological interventions are focused on reducing the frequency of attacks via preventative medications or mitigating the attack or reducing the severity of symptoms at the onset via abortive treatments (Miller, 2012). In migraine research, medication may also be categorised as specific or non-specific (Eigenbrodt et al., 2021). Specific medications include those which are specific to migraine, such as triptans (which bind to serotonin receptors) and gepants (which bind to calcitonin-gene related peptide receptors), and non-specific includes medications which can be used to treat migraine among other conditions, such as non-steroidal anti-inflammatory medications, other general analgesics and anti-emetics (Alsakhairi et al., 2024; Eigenbrodt et al., 2021; Moreno-Ajona et al., 2020). While medication is valuable in improving overall migraine severity and disability, it is not without limitations and caution (Alsakhairi et al., 2024). One particular risk that is frequent among individuals with migraine is medication-overuse headache. According to the International Headache Classification of Headache Disorders-3, medication overuse headache is a chronic daily headache condition characterised by 15 or more headache days per month for more than three months in individuals with a pre-existing headache disorder because of acute medication overuse (Olesen, 2018). Furthermore, research has suggested that medication overuse headache strongly

predicts development of episodic migraine to chronic migraine (Alstadhaug et al., 2017; Lipton et al., 2023).

One proposed mechanism behind the relationship between MOH and migraine chronification is argued to be because of poor acute treatment which causes persistent activation of the pain pathways involved in migraine, in turn enabling central sensitisation (Lipton et al., 2023). However, it is possible that progression may be unrelated to inadequate treatment and rather is inherent in some individuals. In the same regard, a poor response to treatment may be part of chronification process (Lipton et al., 2023). From a qualitative perspective, individuals with migraine report taking excessive medication as an attempt to control pain in attacks which are particularly resistant to medication (Ruiz de Velasco et al., 2003). This lack of reliability of medication effectiveness across attacks is one of the greatest limitations of pharmacological treatments, as there is a significant percentage of attacks which do not respond to treatment, leaving the individual to have to wait for an attack to pass (Dodick, 2005). A study by Roblee et al. (2020) found that 28% of participants with migraine stopped taking their migraine medication due to its lack of efficacy and on average, participants trialled 11 different medicative migraine treatments (Roblee et al., 2020). With each medication, a secondary set of risks are included as each medication comes with a list of side effects which if intolerable or serious, excludes the use of the medication by the individual (Martin & Goldstein, 2005). Some studies highlight that migraineurs may continue medication even after experiencing side effects if it is effective in treating migraine. Gepants have been shown to cause nausea in up to 9% of patients alongside somnolence and constipation in up to 6% (Rissardo & Caprara, 2022). Research on Triptans has shown more varied and concerning side effects, particularly in individuals at risk for

cardiovascular disease and more general cardiac problems (Liu et al., 2024). Such individuals are at risk for coronary artery dissection, angina, and myocardial infarction (Liu et al., 2024). Alongside this, gastrointestinal symptoms and disorders are frequently reported with triptan use (Liu et al., 2024).

1.6.2 Psychological and Behavioural Treatments

The overlap between cognition and pain further encourages the development and use of psychological treatments in migraine patients. By acknowledging that the perception of pain is shaped by cognitive, affective and sensory processes, the utility of psychological therapies in pain management becomes apparent (Ehde et al., 2014; Wiech et al., 2008). Furthermore, the need for non-pharmacological treatments and their utility are frequently observed in qualitative research (Morgan et al., 2016; Urtecho et al., 2023). Research has shown that pain catastrophising, including negative thoughts about the severity of pain and its potential impact, is associated with greater impairment irrespective of experienced pain severity and affective disorders such as depression (Edwards et al., 2011). As such, targeting and reframing negative thoughts, beliefs and responses to pain can significantly reduce the levels of pain, disability, and impact on mood (Ehde et al., 2014). Therapies which effectively target maladaptive cognitions and emotions associated with pain include Cognitive Behavioural Therapy (CBT), Dialectical Behavioural Therapy (DBT) and mindfulness based interventions such as mindfulness meditation (Garland et al., 2014; Hilton et al., 2017; Kabat-Zinn et al., 1985; Khoo et al., 2019; Norman-Nott et al., 2022; Sysko et al., 2016; Williams et al., 2020; Zeidan et al., 2011). Cognitive behavioural therapy aims to identify and modify maladaptive pain related thoughts and behaviours (Ehde et al., 2014). Whereas DBT aims to target emotional dysregulation through emotional skills training, which in turn can improve the

intensity of pain as well as improving coping behaviours (Norman-Nott et al., 2022). Mindfulness-based interventions recognise the role of attention in pain perception and trains the individual to detach affectively from the experience of pain by observing the pain attentively and acceptingly, with effort to maintain nonevaluative cognitive control while observing pain (Kabat-Zinn, 1985; Hilton et al., 2017; Zeidan et al., 2011).

CBT may improve migraine outcomes through reframing unhelpful pain-related beliefs, thoughts, and responses to the migraine (Amatrudo et al., 2023; Bond et al., 2015). A systematic review and meta-analysis by Bae et al. (2021) found that CBT in migraine can reduce migraine frequency and disability (measured through MIDAS and HIT). Another study by Klan et al. (2022) observed that outcomes of headache days, headache-related disability, emotional distress, and self-efficacy were improved by a migraine-specific CBT programme that combined trigger and stress management, coping with fear of migraine attacks and relaxation training.

Evidence for the effectiveness of mindfulness-based interventions in migraine is mixed. A recent systematic review and meta-analysis by Prohaska and Matthias (2023) found that most studies observed no benefit of mindfulness-based stress reduction in migraine prevention. Similarly, in another study, mindfulness meditation was comparable with migraine education in decreasing attack frequency (Wells et al., 2020). These findings are contrasted by research by Simshäuser et al. (2021) who observed reduced headache frequency and improvements in psychological outcomes including pain catastrophising. However, therapy that combines cognitive behavioural facets with mindfulness-based interventions have proven to be effective in reducing migraine disability, particularly in episodic migraineurs (Seng et al., 2019; 2021). Research on DBT is less studied in migraine

populations. However, research has found that DBT can improve cognitive functioning and some success has been observed in reducing chronic pain in individuals with gastrointestinal disorders (Sysko et al., 2016; Vijayapriya & Tamarana, 2023).

Alongside pharmacological and psychological treatments, some studies suggest the efficacy of lifestyle management in migraine management, although this is also a developing area of research (Quartetti et al., 2025). Research has found that individuals with chronic migraine display less regular lifestyle behaviours compared to those with episodic migraine (Woldeamanuel & Crown, 2016). As well as this, multiple studies have observed associations of obesity and diet, sleep comorbidities, dehydration, caffeine intake, alcohol consumption, smoking and physical activity with migraine frequency and severity (Agbetou & Adoukonou, 2022). One such lifestyle management framework is the SEEDS approach to migraine which encourages individuals with migraine to maintain their sleep, exercise, eating habits, diary recording, and stress management (Roblee & Starling, 2019). Irrespective of the debate on prodromal symptoms versus triggers, it is likely that both theoretical frameworks are correct whereby poor sleep, poor diet and lack of exercise make the migraineur more vulnerable to an attack and related sleep and diet symptoms (Agbetou & Adoukonou, 2022; Karsan & Goadsby, 2017).

Finally, the use of psychological and behavioural interventions in migraine management is recommended by the American Headache Society and European Headache Federation, which both include psychological therapies and lifestyle management as important factors in primary management of migraine (Ailani et al., 2021; Steiner et al., 2021). Overall, research on psychological and behavioural treatments in migraine is promising; however, more research is needed to tailor and

optimise therapies to individuals with episodic and chronic migraine. Multimodal approaches integrating CBT, mindfulness-based interventions, relaxation techniques, lifestyle management, migraine education, and migraine-specific pharmacological treatments are increasingly recognised as valuable components of comprehensive migraine care. Such approaches may be particularly valuable for more severe, difficult to manage cases, as recommended by international consensus guidelines (Ailani et al., 2021; Steiner et al., 2021).

1.7 Thesis Overview

The primary aim of this thesis is to investigate migraine as a cyclical neurological disorder with biological, psychological, behavioural, and social manifestations. The conceptual foundation of this research draws on multiple related but distinct bodies of literature.

The first is the chronobiological framework, which emphasises the temporal organisation of biological processes. Within this framework, health and illness are understood partly in terms of how well an individual's endogenous rhythms align with the external light–dark cycle. Although the sleep–wake cycle is the most visible circadian rhythm, its timing varies between individuals due to genetic differences that influence circadian phase of entrainment (Roenneberg et al., 2019). These differences result in chronotype phenotypes such as early and late types, where early chronotypes sleep and wake earlier than average, and late chronotypes later than average. Chronotype reflects not only sleep timing but broader circadian rhythmicity in behaviours implicated in migraine, such as sleep patterns, activity and dietary timing (Roenneberg et al., 2019; Takahashi et al., 2018). Overlap between circadian-

regulated behaviours and core migraine-related symptoms (e.g., altered sleep, changes in appetite) likely reflects the central role of the hypothalamus in both circadian regulation and migraine pathophysiology. In the same regard, the reliance of light in circadian entrainment coupled with the sensitivity to light stimuli in individuals with migraine may increase the risk of circadian misalignment due to the abnormalities in photic perception (Golombek & Rosenstein, 2010; Nosedá & Burstein., 2011).

The second framework concerns contemporary migraine research suggesting that sleep and feeding disturbances may not act as external triggers or aggravating factors but represent manifestations of an early phase of the migraine attack—the prodromal or premonitory phase (Karsan & Goadsby, 2018). This understanding further suggests a postdrome phase following the migraine pain where the individual experiences cognitive difficulties among other symptoms (Bose et al., 2018). In this regard, migraine is cyclical, with symptoms beginning in the prodrome phase and returning to normal following the prodrome. Within a chronobiological perspective, misalignment between behaviour and the external light–dark cycle constitutes circadian misalignment, which has been associated with adverse health outcomes not limited to obesity and cardiovascular disease. A central question of this thesis, therefore, is whether migraineurs are particularly susceptible to circadian misalignment, as reflected in their sleep and dietary behaviours and is this associated with increased migraine frequency.

Chapter Two of this thesis reviews the literature on neuropsychological functioning in adult samples of individuals with migraine. As there is a mixed consensus on cognition, a formal synthesis of the empirical literature was needed to create a neuropsychological profile of migraine. It is hoped that this will shape clinical

procedure in cognitive testing and highlight key areas for therapeutic interventions.

Chapter Three investigates cross-sectionally whether there are any differences in levels of sleep and eating behaviours between individuals with migraine and healthy non-migraine individuals. It was hoped that this would highlight whether behavioural differences in sleep and eating are associated with migraine diagnosis as a potential area for intervention. **Chapter Four** focused on the subjective impact of migraine at the individual level by using a qualitative approach to data analysis using thematic analysis. It was important for this research to ensure that the day-to-day lived experience wasn't reduced by the positivist approach taken in the other empirical chapters included in this thesis. **Chapter Five** assesses the predictive value of longitudinal actigraphy measurements of sleep, activity and heart rate alongside self-reported sleep, perceived body temperature (feeling hotter or colder than usual), increased or reduced appetite, stress, fatigue and mood on migraine onset and migraine severity within and between individuals with migraine. This study also investigated whether there were differences in neuropsychological functioning between phases, the interictal migraine-free phase and 24 and 48 hours following a migraine attack in the postdrome. The motivation behind this chapter was to investigate the predictive value of the variables measured as a means to improve migraine treatment through informed interventions targeted at modifying important predictors or using the predictors as a temporal marker for abortive medication which are more effective in the early stages of an attack. Alongside this, the variance in cognitive functioning in migraine may be explained by temporary, cyclic cognitive impairment, which may return to normal following the prodrome. It is hoped that a longitudinal design may shed further light on this topic and enable greater therapeutic interventions for non-painful symptoms relating to cognition. A brief chapter on the qualitative experience of participating in the longitudinal study

presented in the previous chapter is presented in **Chapter Six**. Finally, a general discussion of the overall results from each chapter is presented in **Chapter Seven** alongside limitations to the present research and directions for research moving forward.

Chapter Two

In Search of a Neuropsychological Profile for Migraine: A Scoping Review

Richardson, S., & Diaz-Orueta, U. (2024). In search of a neuropsychological profile for migraine: A scoping review. *European journal of pain (London, England)*, 28(7), 1033–1068. <https://doi.org/10.1002/ejp.2244>

Abstract

Migraine is commonly overlooked by the general population and by professionals in research and practice as a novel head pain rather than recognised as a cyclic disorder of the nervous system, which is defined by significant abnormal psychological, physiological, and neurological pathologies. Moreover, it is difficult to grasp the neuropsychological profile of migraineurs due to the cyclic nature of the disorder. With this in mind, a scoping review of the literature was conducted with the goal of identifying studies focusing on the characterization of cognitive domains associated with deficits in migraine. Databases including PubMed, PsychInfo, Scopus, EMBASE and OpenGrey were searched for studies published from January 1st, 2006, to November 30th, 2022. Following the review process, 52 eligible studies were included in the review. While some studies consistently report problems in cognitive domains such as associative learning and memory; auditory processing and memory; abnormal attention processing, lower processing speed, problems across a range of executive functions (such as decision making, cognitive flexibility or prospective memory) and some limited indications of deficits in spatial navigation; other studies find no significant differences when compared to controls. Lack of consistence across studies in sample selection and sizes, type of migraine, ictal phase, etc. may affect clarity and consistency of results observed. Further research properly addressing the role of age, chronicity, comorbidities, ictal phase of functioning observed is needed alongside increasing consistency across diverse neuropsychological assessment protocols.

2.1 Introduction

Migraine is commonly overlooked as a novel head pain by the general population and professionals rather than recognised as being a complex disorder of the nervous system that it is. Migraine is frequent, being the third leading cause of disability worldwide (Meng et al., 2018; Steiner et al., 2015; Stovner et al., 2018). Albeit common among the general population with a conservative 14% reported to be suffering from the disorder worldwide, migraine is still largely unknown (Saylor & Steiner, Stovner et al., 2018). Many of the functional and causal mechanisms are not clearly established; and migraine treatment, despite continuously developing alongside theory and technology, remains inadequate for many (Goadsby, 2015; Goadsby et al., 2017; Qubty & Patniyot, 2020). In relation to this, many inadequacies can be attributed to large proportions of literature and practice emphasising and focusing primarily on relieving migraine pain while overlooking the neurological, psychological, and behavioural events that occur prior, during and following the onset of the characteristic pain (Burch & Rayhill, 2021; Karsan & Goadsby, 2021; Goadsby et al., 2002). This may be largely due to previous research and consensus focusing on migraine as a vascular rather than neurological disorder (Goadsby, 2015). Furthermore, pharmacological treatment contributes to increased frequency of medication overuse headache and chronic, rhythmic migraine (Westergaard et al., 2014; Diener et al., 2020).

The migraine cycle begins with the premonitory, preictal phase in which individuals experience significant changes in neurological, physiological, and psychological functioning (Goadsby et al., 2017; Green & Muskin, 2013; Karson & Goadsby, 2021; Laurell et al., 2016; Qubty & Patniyot, 2020). Such dysfunction is often present in the form of sensory aura, intense fatigue, satiety changes,

deregulatory mood, gastrointestinal distress, polyuria, yawning, kinesiophobia, subcutaneous allodynia, phonophobia and photophobia (Karsan & Goadsby, 2018; Wang et al, 2021). Such symptoms may persist throughout the ictal stages and are typically not the focus of research or intervention.

Imaging studies have demonstrated an increased activation in regulatory areas of the migraine brain during the ictal stages of an attack, including the hypothalamus, thalamus, periaqueductal grey region, dorsal pons, and the brainstem (Goadsby et al., 2017; Karsan et al., 2021; Maniyar et al., 2014). A review by David et al. (2020) found that neuroimaging revealed increased activation and abnormal functioning of cortical areas intrinsic to memory processing and formation, the integration of sensory information and temporal cortical areas responsible for language and visuospatial functioning (see also Ravishankar & Demakis, 2007). Similarly, a systematic review found abnormal functional connectivity in various networks including “salience, sensorimotor, executive, attention, limbic and default mode networks, and networks related to visual processing” (Chong et al., 2019: p6). A review by Liu et al. (2018) further suggests abnormal functional connectivity of the hippocampus at resting state in migraineurs.

Frequency of headache and migraine has continued to increase throughout the 21st century alongside the development of technology and increase in work-related fatigue and stress (Goadsby et al., 2021). According to the International Headache Society's (2018) *International Classification of Headache Disorders*, chronic migraine is classified as equal to or upwards from 15 migraine days per month. This subsequently sums to 50% of the chronic migraineur's lifetime lost to disability albeit physiological and pain related or more intertwined, cognitive, and psychological impairment (Karsan & Goadsby, 2021). Nevertheless, migraine and

headache frequency continue to increase and appear in younger populations, with children and adolescents reporting headache (Nieswand et al., 2020).

However, the neuropsychological and cognitive literature on migraine is laden with contradictory findings, with alternative reviews suggesting no significant cognitive dysfunction or long-term decline among the population (Gil-Gouveia & Martins, 2019; Rist & Kurth, 2013). In a previous systematic review, De Araujo et al. (2012) reported defective performance in memory, attention and processing speed for those migraineurs attended in neurological care centres, but not for those in the community (similar to findings from Vuralli et al., 2018).

Research has further suggested migraine to be a significant predictor of all-cause dementia (Lee et al., 2021; Morton et al., 2019). A concerning finding that opposes existing research reporting no significant decline in cognitive functioning among migraineurs. This link between migraine and an increased risk for all cause dementia (i.e. Alzheimer's, Vascular Dementia, and so on) has been evidenced in a recent meta-analysis by Gu et al. (2022), although another review by Begasse de Dhaem and Robbins (2022) finds that relationship between migraine and dementia unlikely. It is possible that more distinction on whether research pertains to pre, post ictal or interictal functioning is needed as it is plausible that much observed dysfunction is transient and reversible (Gil-Gouveia et al., 2019; Gil-Gouveia & Martins, 2015). Furthermore, varied durations and temporal presentations of the migraine cycle within groups may distort findings and potential cyclic dysfunction relative to ictal and interictal stages. For example, Vuralli et al. (2018) found that poor cognitive performance during migraine attacks is more clearly established, while interictal data are conflicting. A recent meta-analysis by Braganza et al. (2022), on the contrary, showed a moderate, negative effect on complex attention,

immediate and delayed memory, spatial cognition and executive functioning during the interictal period, although report that lack of performance validity tests and limited data on mood symptomatology in the reviewed studies could overestimate the magnitude of effect.

Regardless of such findings depicting complex brain activity and recognition of migraine as a complex neurological disorder, limited research exists on the cognitive and neuropsychological functioning of migraine, ultimately leaving a gap in the migraine literature and subsequently in the migraine treatment (Karsan & Goadsby, 2021). Pinotti et al. (2022) performed a meta-analysis restricted to search for deficits in executive functions, showing worse performance for migraine patients in executive functions when compared to healthy controls (including attention, working memory and mental flexibility), with no difference reported between migraine with and without aura. In terms of tests that can be sensitive to cognitive alterations in migraine, Vallesi (2020) conducted a meta-analysis showing that Trail Making Test showed adequate sensitivity for the detection of cognitive alterations in migraine, which opens the door for further research on the establishment of agreements towards a neuropsychological assessment protocol for migraine.

However, for such a detailed assessment protocol to be established, there is a need for existing research to be synthesised to enable a more insightful narrative of the cognitive and neuropsychological functions impaired in the migraine population. This would enable targeted interventions to relieve cognitive and behavioural impairment that is often dismissed despite contributing significantly to the condition's phenotype particularly during prodromal, aura and postdrome phases (Karsan & Goadsby, 2021). It is with this in mind that this scoping review of the literature was conducted, with the goal of identifying and trying to establish a

comprehensive profile of all cognitive domains associated to deficits in individuals suffering from migraine, regardless of pre-established misconceptions of the condition, and an aim to provide further clarity in the delimitation of which and how are those cognitive domains mainly affected in individuals with migraine.

It is hoped that this synthesised narrative of the neuropsychological profile in migraine will pave the way for further research on establishing an adequate neuropsychological assessment protocol for migraine, as well as for expanding knowledge on the disorder; but also providing alternative, psychology-based interventions and treatments by emphasising the abnormal and complex neuropsychological functioning observed at different points in the migraine cycle (which may often occur multiple times during a 30-day/ 1 month period).

2.2 Methods

2.2.1. Search Strategy

To ensure credibility, the search methods used in this scoping review were developed and applied with congruence to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) criteria (Page et al., 2021). In addition, the recommendations by Peters et al. (2015) on how to conduct a scoping review were taken into consideration. Due to the significant variation in measurements used in the reviewed studies it was decided that meta-analysis would not be viable given the extensive methodological heterogeneity. Furthermore, as the purpose of this research is to comprehensively depict neuropsychological functioning in migraine, a scoping review was apt and broadened the scope of the research. Despite the existence of previous systematic reviews related to this topic, the laden of contradictory results, the early stage of the emerging research in this

area and the need to clarify concepts, following the guidelines by Munn et al. (2018), justified the need to conduct this scoping review. To acquire studies used in this review, databases including PubMed, PsychInfo, Scopus and EMBASE and OpenGrey were methodologically searched using the following syntax: (Migraine) AND (cognition OR neuropsychology OR neuropsychological OR neurobehavioural OR neurocognitive) AND ("decision making" OR attention OR mood OR memory OR "spatial behaviour" OR perception OR sleep). For the purpose of this review and to capture the current scope of the literature, research published in the last 16 years (from January 1st, 2006, to November 30th, 2022) were included.

2.2.2. Selection, Screening and Extraction

The search from the combined databases returned a total of 2,271 references which were compiled and assessed for duplicates. A total of 1,742 eligible studies remained following extraction of duplicate references. The 1,742 references were further uploaded to Rayyan Systems Inc (www.Rayyan.ai), an online software for collaborative systematic reviews. To minimise bias, the studies were divided and screened independently by each of the authors. Inclusion criteria for the review included adults over the age of 18 years experiencing primary migraine and use of clinically administered standardised measures of cognition and neuropsychological functioning. A significant number of studies were excluded with regard to the inclusion criteria of this study. Many references were excluded due to studies focusing on other primary headache disorders (not migraine) or secondary headache attributed to a causal or identifiable factor. Similarly, many studies were excluded due to lack of neuropsychological or cognitive measures. Such studies were predominantly focused on genetics, pharmacology and neuroscience and were further outside the scope of the review. Following the screening process, a total of 89

studies were inspected further to ensure relevance to the review and overall credibility.

After thoroughly screening each of the remaining studies, 32 were excluded. While many of these studies claimed to investigate cognition, in 17 of them no cognitive measures were used (instead, such studies focused on contrast discrimination, saccades or sensory thresholds), 11 included self-report measures on cognition, two had mixed samples with different conditions and the remaining two included participants under 18 years old. This quality review process led to a number of 52 eligible studies that were included in the review (see Figure 2.1).

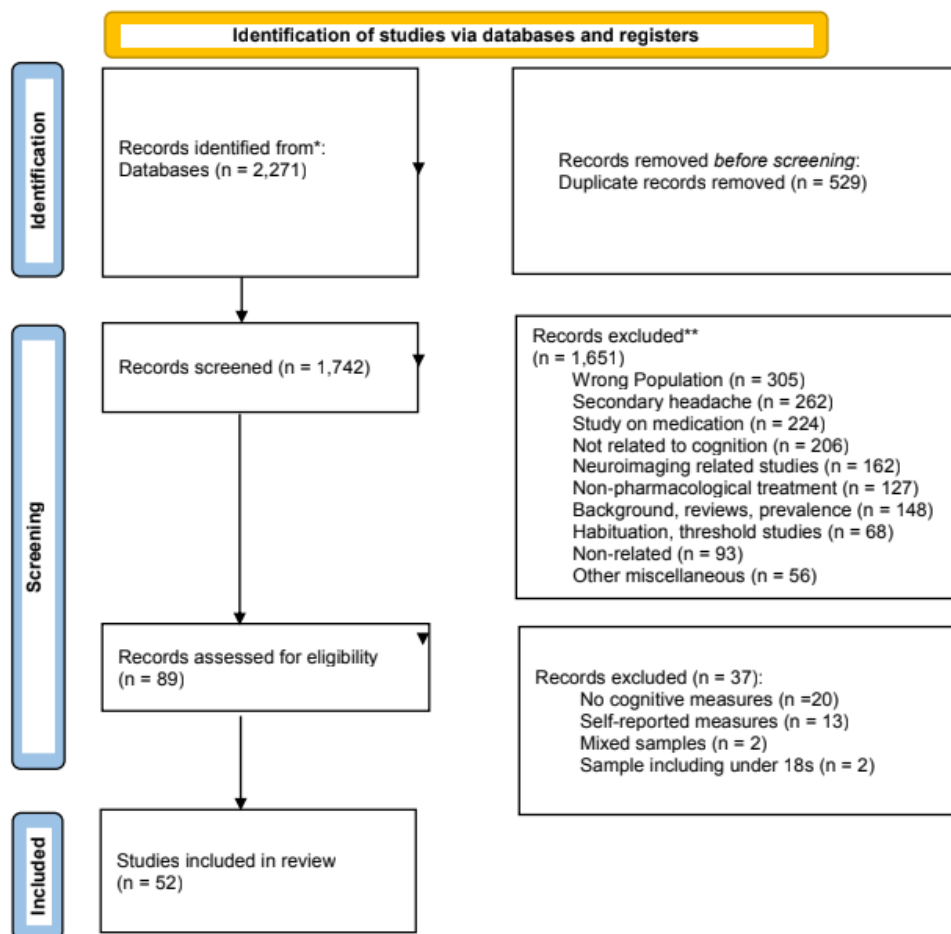


Figure 2.1. PRISMA flow diagram of the exclusion process.

2.3 Results

2.3.1. Global Cognitive Functioning Screening Measures

Some of the studies reviewed informed on global cognitive performance based on regularly used cognitive screening tasks such as the Montreal Cognitive Assessment (MoCA) and the Mini Mental State Examination (MMSE). Results from these studies were mixed, with the majority of studies finding significant differences on the MoCA between migraineurs and controls, with worse results for migraineurs with aura and chronic migraineurs.

2.3.1.1. *Studies focused on the Montreal Cognitive Assessment (MoCA)*

Santangelo et al. (2016) found, in a sample of 72 migraine patients (without aura, in the inter-ictal stage) versus 72 healthy controls, an overall worse performance in migraineurs both for the total MoCA score and for most sub scores (except for language and orientation sub scores, where no significant differences were found). Huang et al. (2017) showed similar results but with slight differences, with a worse performance for migraineurs in both language and orientation, but not in visuospatial and attention components of the MoCA. Correlation analysis in this study found that migraine duration was significantly and negatively associated with overall MoCA scores (-0.446 ($p < .01$), as well as subdomains of language, executive functions, calculation and memory. In addition to this, Ferreira et al. (2018) found significantly lower MoCA scores for the chronic migraine group (mean= 24.4) in comparison to controls (mean = 26.7 ($p < .001$). Moreover, chronic migraine was further independently associated with a lower MoCA performance before and after controlling for medication use, anxiety, sleep, and depression. Tunç et al. (2018) reported similarly that MoCA scores were positively associated with migraine

frequency ($p < .01$), reinforcing the idea that those with chronic migraine may be more likely to experience impaired cognitive performance.

Focusing on studies within migraine subgroups, Latysheva et al. (2020) found no significant differences on MoCA scores between episodic ($n = 44$) and chronic migraineurs ($n = 144$) or between migraineurs with and without medication overuse headache. However, they found that 18% of chronic migraineurs in the sample met the criteria for mild cognitive impairment compared to 6% of episodic migraineurs. Moreover, anxiety levels in the sample correlated positively with the MoCA, suggesting anxiety enhanced performance. Separately, comparing migraineurs with, without aura and healthy controls, Tunç et al. (2018) reported that significantly worse performance on total MoCA scores was observed only in migraineurs with aura (21.7 ± 5), with no differences between migraineurs without aura (24.9 ± 3.5) and healthy controls (24.4 ± 3.8).

2.3.1.2. Studies focused on the Mini Mental State Examination (MMSE)

Another range of studies using the Mini Mental State Examination as the core assessment did not show differences in global cognition between migraineurs and healthy controls (Rist et al, 2011, Wang et al., (2014) or between groups of migraineurs with or without medication use over time and healthy controls (Baars et al., 2010). Performance on the MMSE within groups, based on migraine frequency, was also similar, with no significant differences observed between individuals with episodic and chronic migraine (Latysheva et al, 2020).

Contrary to these findings, Kalaydijan et al. (2007), using a longitudinal design, found that mean MMSE values were significantly greater for the migraine group compared to healthy controls ($p < .05$). However, the sample sizes in this study were uneven (with 204 participants with migraine and 1244 healthy controls),

and the control group was older (52.7 ($\pm$ 15.7) years) than the migraine group (47.5 ($\pm$ 12.5) years), which may suggest some age-related cognitive decline in the control group.

2.3.1.3. Studies using both MMSE and MoCA

General findings above, with significant differences for the MoCA but not for the MMSE were also supported by Santos-Lasaosa et al. (2013), who found significantly lower scores on the MoCA in the chronic migraine group compared to controls ($p < .005$), but not for the MMSE (see also, Martins et al., 2012; 2020).

2.3.2. Perception

Up to 13 studies included in this review included measures and outcomes for perceptual functions in migraineurs. Due to the strong interconnection between perceptual performance and cognitive processes, it was deemed necessary to take the outcomes of these studies into consideration. Below, we divide them between those focused on visual and auditory perception.

2.3.2.1 Studies focused on Visual Perception

Here we present studies focused on diverse visual phenomena linked to migraine (i.e. photophobia, perceived illusory motion, etc.) and their links with some cognitive processes such as attention.

Using a cross-sectional mixed design Koppen et al. (2011) examined perceptual organisation and attention using a sample of clinical outpatient non-frequent and frequent migraineurs ($n= 16$), and healthy controls ($n= 18$) using a Global-Local task (participants were presented with hierarchically organised visual figures, in which a larger -global- letter was composed of smaller -local- letters). No significant differences were observed between migraineurs and controls, or between

baseline and postdrome functioning in the migraine group. However, the control group showed significantly faster reaction times to global stimuli compared to local ($p < .05$), a performance that was not replicated in the migraine group. Koppen et al. (2011) suggest that visual channels tuned to low spatial frequency ranges of migraineurs may be less sensitive between attacks and as such processing through these channels may be impaired. Similarly, Kriegler et al. (2020), using a greyscale task, found that migraineurs performed significantly worse than controls and performed similar to that observed in unilateral neglect patients. These authors attributed this defective performance in migraineurs to an impaired attention to luminosity as a result of sensitivity to high frequencies of visual stimuli rather than size perception.

Separately, Guo et al. (2019) examined between and within group differences in visual attention among migraineurs using a three-stimulus visual oddball paradigm and found female migraineurs to have greater perceptual impairment in attentive visual processing in comparison to male migraineurs and to female controls.

In a longitudinal, repeated measures study, Luedtke & Edlhaime (2021) found significant differences between migraineurs, and healthy controls on a Laterality Recognition Task. Migraineurs performed significantly worse in identifying images with both and leftward ($p < .05$) and rightward bias ($p < .01$) compared to healthy controls. No significant differences in mean response time were found. Due to the longitudinal design, these researchers were able to examine differences in response times across migraine phases; and highlighted the cyclic nature of the condition in which perceptual impairment seems to be greatest from the 24-hour period before to the 24 hours after a migraine attack.

When a motor or movement component is introduced, the results go in a similar direction. According to findings by McKendrick et al. (2006), visual motion perception is impaired interictally in people with migraine when stimuli are embedded in noise using a Global Motion paradigm. Results from this study found that the mean global motion coherence threshold was significantly higher in the migraine group in comparison to controls ($t(54) = 2.1, p < .05$), suggesting interictally impaired visual motion perception when stimuli are embedded in noise in migraineurs, an impairment that is irrespective of cognition (based on the results using the Repeatable Battery for the Assessment of Neuropsychological Status - RBANS) and medication.

Another study by Tibber et al. (2014) supports the findings of impaired visual motion perception in migraineurs using the Motion Discrimination Task with embedded noise. In comparison to controls ($n = 22$), migraineurs ($n = 22$) displayed significantly higher mean motion coherence thresholds ($24\% \pm 1.8\%$, $32\% \pm 3.3\%$ respectively, ($t(37) = -2.37, p < .05$, Cohen's $d = .78$)). Contrary to the above, one study by Battista et al. (2010) found that migraineurs performed significantly better than controls on motion discrimination tasks with increased inhibition and ability to suppress competing visual stimuli.

An additional number of studies examined the differences between migraineurs and healthy controls in relation to perceived illusory motion. In a study by Shepherd (2006), induced motion aftereffects lasted significantly longer in the migraine group compared to controls ($p < .001$). No significant differences were observed between migraineurs with and without aura. A study by Miller et al. (2015) further examined vection perception using a motion platform and a forced choice task. This study used inertial nulling (IN), which is a technique wherein visual and

inertial motions are presented simultaneously, with the modalities presented in opposition in order to determine the visual stimulus that produces perceived vection that is nulled by the inertial movement. Results from this study found that migraineurs required significantly greater nulling velocity (Mean = 1.18 ± 0.51 cm/s) to eliminate the perception of motion in comparison to healthy controls (Mean: -0.008 ± 0.56 cm/s, $p < .05$). Such results of increased vection or perceived illusory motion in migraineurs are suggested as an explanatory mechanism for the increased frequency of vertigo, nausea, dizziness, and motion sickness in this population (Shepherd, 2006; Miller et al, 2015). A more recent study by O'Hare et al. (2018) found no difference in postural sway or head movements between healthy controls ($n = 13$) and migraineurs ($n = 15$) in response to an illusory motion condition using a Pattern Glare Test. However, this study required participants to verbally answer the Pattern Glare test, and cognitive tasks like that have been shown to counteract the effects of illusory motion (Swan et al., 2007, as cited in O'Hare et al. 2018).

Based on the findings of the studies included in this review, perceptual functions are impaired in migraine. Furthermore, in Chu et al. (2011), both migraineurs with and without photophobia experienced significantly more visual discomfort than controls on a Visual Discomfort Test, highlighting an increased sensitivity to visual stimuli. Moreover, post hoc analysis revealed greater discomfort in migraineurs with photophobia than in those without. The adversity to perceptual stimuli and the perceptual impairments highlighted in this review encourage further exploration of perceptual processing in migraine as an important implication in migraine neuropsychology and therapy.

Further research is needed to establish to what extent this evidenced general sensitivity between migraine attacks may influence performance on a wide array of

tasks that require visual processing (including neuropsychological assessment tools for attention, memory, visuospatial or executive functions that may rely on visually presented materials).

2.3.2.2. Studies focused on auditory perception

A few studies assessed auditory perception in migraineurs. In Agessi et al. (2014), with a cross sectional between groups design, migraineurs performed significantly worse on the Gaps in Noise Test ($p < .01$; $p < .05$) and the Duration Pattern Test ($p < .001$) compared to non- migraine controls. These results suggest impaired auditory and temporal processing in migraineurs, an impairment whose mechanism needs to be explored further to examine the role of memory and attention on performance. Zhang et al. (2012) also suggest interictally impaired temporal perception in migraineurs. Using a Temporal Reduction Task, migraineurs ($n = 27$) significantly overestimated stimulus presentation time when compared to healthy non migraine controls ($n = 27$) for the of 1 second ($p < .00$) and 5 second ($p < .01$) interstimulus level in the 600ms condition. However, no impairment of time discrimination in the longer conditions of 3 seconds and 5 seconds was found. However, further correlation analysis found no significant relationship between time discrimination performance (time estimations) and cognitive performance or mood in migraineurs or controls.

2.3.3. Attention

The studies in this review that measured attention showed a trend towards established attention deficits in migraine populations compared to healthy controls.

A number of studies in this review found significant impairment in migraineurs using the Stroop test. Ferreira et al. (2018) found that mean scores on the Stroop test were significantly lower in the migraine group compared to controls

($p < .001$). In a regression analysis Stroop scores were significantly associated with migraine status ($p < .05$). In this study, Stroop scores were not associated with topiramate use, anxiety, depression, or poor sleep. Poormina et al. (2017) also found that mean time needed to complete the Stroop test was significantly higher for migraineurs (132.17 ± 7.027 seconds) compared to controls (106.40 ± 15.87 seconds, ($p < .001$)), thus suggesting inter-ictal attention and processing speed impairments in the migraine population. This attentional deficit may further worsen as a migraine cycle progresses. In a sample of episodic migraineurs without aura, Gil-Gouveia, Oliveira, and Martins (2015) found that migraineurs performed significantly poorer on tests of attention during a migraine attack compared to baseline, interictal functioning. During an attack, scores on the Stroop Words (reading) (77.6 ± 21.0) were significantly lower than that observed at baseline (90.6 ± 17.1 ($p < .05$)) following adjustment for multiple comparisons, suggesting a mild selective attention deficit during an attack.

Similarly, Su et al. (2021) found significant differences in response time, with migraineurs displaying longer reaction times, but reported no significant differences in Stroop accuracy between migraineurs and controls. However, Quadros et al, (2020) found no significant differences between any phases of migraine (inter-ictal, preictal, ictal or postictal) using the Stroop test.

Impaired attention was further observed in samples with high levels of formal education. In a case-control study, Yannick et al. (2015) found that migraineurs performed worse on the Delis-Kaplan Executive-Functions System (D-KEFS) Colour-word Interference test. In this study, migraineurs displayed significantly lower mean interference scores (-4.04 ± 7.08) than controls (-1.31 ± 7.73 ; $p < .05$).

Levels of anxiety and depression did not significantly correlate with interference in either group (Yannick et al. 2015).

In a case-control study, using the Attentional Networks Test, Chen et al. (2021) observed significant differences between groups on reaction times ($F = 84.085$, $p < 0.001$), but not on levels of accuracy. Contrary to previous studies, no significant differences were observed between groups on any of the Stroop Test tasks. However, the sample in Chen et al. (2021) was smaller than in other studies discussed above.

One single study seemed to point, at least partially, to a better attentional performance in migraineurs, but only to negatively biased images. Puschmann and Sommer (2011) found that healthy controls demonstrated significantly greater attentional bias for negative stimuli using the emotional Stroop test whereby performance was directly impaired by negative affective images. This attentional bias was not present in the migraine group who performed better on the negative condition of the task compared to neutral or positive conditions. While more research is needed to further understand this mechanism and establish the reliability of these findings, Puschmann and Sommer (2011) suggest the results of the study may relate to the frequent reliance of avoidance behaviours within the disorder.

2.3.4. Memory

Memory appears to be one of the most affected cognitive domains found across 15 of the studies included in this review. Studies reviewed consistently showed a worse performance in individuals with migraine, regardless of the presence of aura in some cases, and even in interictal, pain free periods. Interestingly, this is the most studied cognitive domain, with studies showing differences not only based

on migraine phase or type, but also how gender, mood or sleep may be associated with memory performance. Similar to other cognitive domains, a series of studies showed no significant migraine specific memory performance. As with other cognitive domains, there was significant variation between the measures used among the studies, so the limitations of these neuropsychological measurements is an additional factor that needs to be considered.

First, starting with studies focused on differences between migraineurs and healthy controls, Santos-Lasaosa et al. (2013) found significant worse performance on chronic migraineurs ($n = 30$) compared to healthy controls ($n = 30$) on the Memory Alteration Test (43.76 ± 3.21 versus 48.83 ± 1.89 , ($p < .005$)). Further significant differences were observed between subdomains of the test including short-term memory ($p < .005$), semantic memory ($p < .05$), free recall ($p < .005$) and facilitated recall ($p < .005$). Similarly, Raimo et al. (2022) showed that chronic migraineurs displayed significantly poorer prose memory (delayed recall) and interference memory at 30 seconds compared to controls.

Another cross-sectional study by Öze et al. (2017) examined differences of performance on the Rutgers Acquired Equivalence task between groups of migraineurs ($n = 22$) and healthy controls ($n = 22$). Results from this study found that migraineurs made significantly more errors and needed more trials to complete the acquisition phase compared to controls. Similarly, migraineurs performed significantly poorer than controls, suggesting basal ganglia and hippocampal impairment. Using the Rey-Osterreith Complex Figure Test, Huang et al. (2017) found that migraineurs performed significantly poorer on the recall condition of the task compared to non-migraine healthy controls (20.688 ± 6.129 versus 25.316 ± 5.218 , ($p < .05$)). Finally, Lo Buono et al. (2019) found significant worse

performance on the Rey Auditory Verbal Learning Test (RAVLT) for both migraineurs with and without aura, compared to healthy controls.

Second, focusing on different migraine phases, Gil-Gouveia et al. (2015) found significantly decreased performance on the California Verbal Learning Test during migraine attacks compared to interictal functioning between attacks. Overall total learning ($p < .05$), CVLT short-term recall with ($p < .05$) and without ($p < .05$) semantic help, and delayed recall with ($p < .01$) and without ($p < .05$) semantic help were significantly lower during a migraine attack. These findings suggest reversible impairment across various cognitive modalities including memory, learning, and processing speed (Gil-Gouveia et al, 2015).

Third, there is only one study with a focus on memory differences between types of migraineurs. Latysheva et al. (2019) found that performance on RAVLT was significantly poorer in chronic migraineurs when compared to low frequency episodic migraine during interictal, pain free periods of functioning ($p < .01$).

Fourth, in relation to potential gender differences for memory in migraine, a cross-sectional study by Gasbarri et al. (2008) examined differences in recall of arousal and neutral narratives between gender and migraine status (migraineurs and healthy controls). In this study, male and female migraineurs displayed poorer recall of both neutral and arousal conditions than male and female controls. However, this impairment was significantly greater in male migraineurs compared to female migraineurs in both the arousal ($p < .05$) and neutral ($p < .001$) conditions.

Separately, Chu et al. (2020) found a significant association with increasing migraine attack frequency and decreasing performance on the Ascertain Dementia Questionnaire in female migraineurs with aura group, compared to male migraineurs with and without aura, and female migraineurs without aura.

Fifth, regarding associations of memory performance with sleep and mood disorders, Lo Buono et al. (2019) found RAVLT scores were significantly associated with Beck's Depression Inventory and Hamilton Anxiety Rating Scale. Separately, Kim et al. (2020) observed a significant negative association between the Insomnia Severity Index and the RAVLT delayed recall task for the migraine group, suggesting the potential of sleep as a mediating factor of memory impairment in migraine.

Finally, opposing the previously discussed articles, seven studies included in this review did not observe significant memory impairment in migraineurs. Baars et al. (2010), Baschi et al. (2019) and Martins et al. (2020) found no significant differences between migraineurs and healthy controls on memory performance, although the latter observed increased self-reported cognitive complaints in the migraine group compared to controls. Martins et al. (2012) suggested that participants with non-migraine headaches experience greater impairment of semantic and recognition memory than migraineurs, although the inclusion criteria in this study for the non-migraine headache groups remain unclear. Longitudinally, Rist et al. (2011; 2012) also found no significant differences in the rate of memory decline between migraineurs, non-migraine headache and healthy controls over time, using the RAVLT and The East Boston Memory Test. Finally, Kim et al. (2020) found no significant difference between groups of healthy controls, migraineurs or persistent post-traumatic headache (PTH) on measures of immediate and delayed recall from the RAVLT.

To summarise, further research is needed to better understand memory functioning in migraineurs and clarify opposing findings between migraineurs and controls and within migraine sub-groups, as well as the potential effects of other

variables such as gender, mood, sleep and medication intake. This may be achievable using more homogenous measures across future research that aims to examine memory functioning in migraineurs. Finally, the use of appropriate, reliable and valid neuropsychological measures needs to be ensured, in order to accurately identify memory performance features in migraine across the lifespan.

2.3.5. Visuospatial functioning

Only three of the studies included in this review focus on visuospatial abilities in migraine, so results, although promising, are still limited. First, Yetkin-Ozden et al. (2015) examined facial recognition and visuospatial perception in a group of 74 migraine patients with or without aura and 37 healthy controls by means of the Benton Face Recognition Test (BFRT) and Line Orientation Test (LOT). Results showed significantly poorer performance by the migraine group on both tests when compared to controls. Within groups analysis found migraineurs without aura displayed significantly lower mean scores on BFRT when compared to migraineurs with aura ($p < .05$). No difference within groups was found on LOT scores. Further correlation analysis found a significant negative association ($p < .05$) between LOT scores and duration of the condition with those who had migraine for over 10 years, showing lower mean scores (14.84 ± 7.47) in comparison to those with less than 10 years with migraine (17.86 ± 5.57).

Using a motion platform and a forced choice task, Messina et al. (2021) found that migraineurs performed significantly poorer than healthy controls on spatial navigation tasks requiring colour discrimination when compared to angle discrimination (in which no impairment was observed). Using functional magnetic resonance imaging capturing task performance, they found increased activation of brain areas involved in the perception of potentially harmful stimuli (nociception) in

the migraine group. Messina et al. (2021) suggest imaging may highlight adaptive functional plasticity in nociception brain areas that work to maintain otherwise impaired spatial performance.

Finally, in a between-groups study by Karami et al. (2019) using the Bender-Gestalt II with a sample of 32 participants with occipital lobe epilepsy (OLE), 30 with migraine and 31 healthy controls, significant differences were observed on all four components of the BGT-II: copy ($p < .0001$), recall ($p < .0001$), motor ($p < .0001$) and perceptual ($p < .0001$). Post hoc analysis revealed that OLE participants displayed significantly lower scores on all four components when compared to migraine participants. Migraineurs in this study further displayed significantly lower scores on all components compared to healthy controls ($p < .01$)

2.3.6. Executive Functions

In order to present results for executive functions in migraine in a way as clear as possible, we have subdivided the section into results pertaining (1) set shifting and cognitive flexibility, (2) decision making and reasoning, (3) working memory, (4) prospective memory and (5) studies with non-significant or contradictory results.

2.3.6.1. *Set shifting and Cognitive Flexibility*

Schmitz et al. (2008) report that migraineurs had significantly slower reaction times to set shifting using a Visuospatial SWITCH Task compared to controls ($p < .05$). They further found that reaction times to SWITCH-effect in the migraine group were significantly correlated with reduced grey matter density ($p < .05$). Separately, no significant differences however were observed in this study on both the Go-No-Go and Motor Stroop tasks. Similarly, a study by Yannick et al. (2015) found that

migraineurs performed significantly poorer in cognitive flexibility compared to controls. Additionally, a study by Raimo et al. (2022) found that patients with chronic migraine achieved significantly lower scores on tests assessing executive functions including cognitive flexibility, planning, and abstract reasoning with respect to healthy controls.

A subgroup of studies on cognitive flexibility rely on the Trail Making Test or similar tasks. Poormina et al. (2017) found a statistically significant difference in time needed to complete the Trail Making Task B (TMT-B) for migraineurs (54.77 ± 8.169 seconds) compared to healthy controls (56.23 ± 23.457 seconds; $p < .005$). Similarly, Pellegrino-Baena et al. (2018) found significantly poorer performance for migraineurs on TMT-B ($\beta = -0.083$ (95% CI, -0.160; -0.008)) and poorer global z-score ($\beta = -0.077$ (95% CI, -0.152; -0.002)). Lo Buono et al. (2019) reported similar results but indicated that scores on TMT-B were significantly associated with Beck's Depression Inventory and Hamilton Anxiety Rating Scale in the migraine groups ($p < .05$ and $p < .01$ respectively, both with medium effect sizes). These authors suggest that increased levels of depression and anxiety, frequently observed in migraine populations, may exacerbate the risk of executive dysfunction in migraine. Finally, Han et al. (2019) reported that migraine without aura participants performed significantly worse than healthy controls on the Shape Trail Test.

2.3.6.2. Decision Making and Reasoning

Some evidence for impaired decision making among migraineurs was found by Biagianti et al. (2012), with both individuals with chronic and episodic migraine displaying significantly poorer performance on the Iowa Gambling Task compared to healthy controls ($p < .001$), regardless of medication use, suggesting orbito-frontal

impairment in migraineurs. Viticchi et al. (2017) revealed a significant association between migraine frequency and performance on the Raven Colour Progressive Matrices ($R^2 = .3122$; $p < .05$) suggesting poorer performance as attack frequency increased. A similar relationship was observed with length of migraine history with performance on RCPM decreasing over time ($R^2 = .8871$; $p < .001$).

2.3.6.3. Working Memory

In relation to working memory performance in migraine, Santos-Lasaosa et al. (2013) found that chronic migraineurs (17.5 ± 4.28) performed significantly worse than healthy controls (24.26 ± 4.12 ($p < .005$)) in a working memory task. Ferreira et al. (2018) found significant differences in executive functioning on tasks such as Digit Span Forwards and Verbal Fluency Task, with migraineurs performing worse than healthy controls. Regression analysis further found migraine diagnosis to be a significant predictor of poorer performance on these tasks suggesting overall impairment in key domains of executive processes, including working memory.

2.3.6.4. Prospective Memory

For prospective memory, only one study reported results for migraine patients. Santangelo et al. (2018) found a significant difference on measures of the Memory for Intentions Test between groups with migraine without aura performing worse than healthy controls and making significantly more errors. Migraineurs further made significantly more task substitution errors than controls. However, non-parametric methods used in this study do not allow for generalisation of findings to the general population.

2.3.6.5. Studies with non-significant or contradictory results

This review showed five studies with neutral or non-significant findings for migraineurs in the executive functions domain, and one that even had better results for migraineurs.

Schmitz et al. (2008), using a Go-No go task and the Stroop test, found no significant differences in inhibitory processing between the migraine groups and healthy controls. Separately, Koppen et al. (2011) found no significant differences in working memory using the N-back task. More recently, Martins (2020) found no significant differences between mean executive functioning scores in older adults with migraine and healthy age-matched controls. Equivalent results were further observed in Kim et al. (2020), who found no significant differences between healthy controls, migraineurs or post-traumatic headache on TMT A & B, similar to Quadros et al. (2020). Finally, in a different trend, Baschi et al. (2019) found that participants with migraine performed significantly better on the Trail Making Test A and B and the Corsi Block Tapping Test.

Unfortunately, among all the studies eligible for inclusion in this review, few investigated executive functioning between phases of the migraine cycle, and there are limitations with the design seen in these studies alongside others, such as unequal observations and sample sizes per group. Further research is required to clarify whether executive functioning fluctuates throughout the migraine phases and, as some studies seem to point (although with non-significant results, such as Quadros et al., 2020), to clarify whether migraineurs exhibit (or not) overall poorer executive performance in preictal phases when compared to other migraine phases.

Table 0.1. Summary table of the studies included in this review.

Authors and publication year	Study type / Methodology	Participants	Age: Mean (SD)	Measures / techniques used	Summary of main results
Agessi et al. (2014)	Case control Cross-sectional	MwA ($n = 11$) Mw/oA ($n = 15$) HC ($n = 15$)	MwA (29.5 (± 5.8) years) Mw/oA (29.5 (± 6.3) years) HC (29.1 (± 5.0) years)	Gaps in Noise Test (GIN), Duration Pattern Test (DPT) Dichotic Digit Test, (DDT)	Both migraine groups performed significantly poorer on the DPT than controls ($p < .001$). Compared to the control group, Mw/oA group performed significantly poorer for both right ($p < .01$) and left ears ($p < .01$) on the GIN test. While MwA had poorer performance on the GIN test for the left ear ($p < .05$) only compared to HCs. No significant difference on DDT between groups was observed.

					Agessi et al. (2014) suggest central auditory dysfunction as a possible factor in performance differences. Performance could be a result of impaired auditory memory and attention.
Baars et al. (2010)	Case control Longitudinal	M ($n = 99$) HC ($n = 1724$)	M (47.1 (± 12.9) years) HC (51.8 (± 16.6) years)	Mini Mental State Examination (MMSE), The Visual Verbal Learning Test, Stroop Color Word, Test, Letter Digit Substitution Test	Migraine headaches were found to have no effect on any of the cognitive measures. Medication use also had no effect on all cognitive measures. No evidence was found that migraine headaches or use of migraine-related medication are risk or protective factors for cognitive dysfunction or cognitive deterioration over time.
Baschi et al. (2019)	Case control Cross-sectional	MwoA ($n = 21$) HC ($n = 12$)	MwoA (27.9 (± 3.16) years)	CORSI Block Tapping,	Participants with MwoA performed significantly better than HC in both conditions of the CORSI test exploring short ($p < 0.01$)

			HC (29 (± 4.32) years)	Buschke Selective Reminding Test (in supraspan modality), Trail Making Tests A and B (TMTA, TMTB), BDI-SF.	and long-term ($p < 0.01$) visuospatial memory. No significant differences were observed between migraineurs and HC using TMTA and TMTB. No significant difference between groups was found in verbal memory as measured using the Buschke test.
Battista et al. (2010)	Case control Cross-sectional	M ($n = 30$) MwA ($n = 15$) Mw/oA ($n = 15$) HC ($n = 20$)	HC (29.45 (± 6.85) years) M (30.17 (± 7.21) years)	Motion Direction Discrimination task (MDDT), Motion After-effect task (MAET)	Results do not suggest reduced visual motion processing but rather both experiments observed an effect in the opposite direction for the migraine group ($p < .05$) Reports of increased inhibition in migraineurs are not frequent in literature.

Biagianti et al. (2012)	Case control Longitudinal	CMwMOH (<i>n</i> = 40) EM (<i>n</i> = 40) HC (<i>n</i> = 40)	CMwMO (42.7 (±11.0) years) EM (42.1 (±9.7) years) HC (40.7 (±10.3) years)	Clinical Interview Anxiety and Depression Hamilton Scales Severity of Dependence Scale Migraine Disability Assessment questionnaire Iowa Gambling Task (IGT).	Participants with CMwMOH and EM displayed significantly poorer decision making as measured by IGT compared to healthy controls (<i>p</i> < .001). Follow up results from 1 year after the detox, found no significant improvement in IGT scores. No significant differences in orbitofrontal cortex functioning (OFC) were found between the CMwMOH patients who relapsed into medication overuse after detox and those who did not (CM). Results suggest OFC impairment amongst migraineurs and MOH.
Chen et al. (2021)	Case Control Cross-sectional	MwoA (<i>n</i> = 44) HC (<i>n</i> = 20)	MwoA (41.55 (± 12.11) years)	Trail Making Test (Chinese Version),	In the ANT, a significant effect of group (<i>p</i> < .001), cue condition (<i>p</i> < .001) and flanker type (<i>p</i> < .001)

			HC (38.95(± 11.88) years)	Digit Span (forwards and backwards), Stroop Test, Attention Network Test (ANT).	was observed on reaction times (RTs). ANT RTs were significantly longer in the MwoA group compared to HC ($p < 0.001$). Significant differences between groups were observed on raw scores in the efficiency of the executive network ($p < .01$) and the overall mean RT ($p < .05$). Multiple linear regression adjusted for age, gender, literacy, and SAS, SDS showed that the efficiency of the executive network ($p < .01$) and the overall mean RT ($p < .05$) were associated with migraine.
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					Significant group differences were found in the raw scores of TMT-A ($p < 0.001$), TMT-B ($p < 0.001$), TMT-d ($p < .005$), Digit Span Forwards ($p < 0.001$), Digit Span Backwards ($p < 0.001$) and Digit Span Total ($p < 0.001$) Multiple regression analysis adjusted for age, gender, literacy, anxiety and depression, revealed that MwoA was correlated with the scores of TMT-d ($p < .05$) and Digit Span Total ($p < .005$).
Chu et al. (2020)	Case Control Cross-sectional	M ($n = 589$) 1-4 attacks per month ($n = 231$) 5-8 attacks per month ($n = 121$)	M ($45.5 (\pm 30.9)$ years) 1-4 attacks per month ($39.8 (\pm 11.9)$ years) 5-8 attacks per month ($35.7 (\pm 10.7)$ years)	Subjective memory complaints scale Ascertain Dementia 8 (AD8) questionnaire. Beck's Depression Inventory (BDI)	Total subjective memory complaints scores tended to increase with the migraine attack frequency ($p < .05$) in patients with migraine with aura; similar results were obtained for AD8 scores in women with migraine with aura ($p < .05$)

		9-14 attacks per month ($n = 109$) 15+ attacks per month ($n = 128$) HC ($n = 80$)	9-14 attacks per month ($36.7 (\pm 12.1)$ years) 15 or more attacks per month ($40.2 (\pm 11.4)$ years) HC ($41.4 (\pm 12.8)$ years)	The Pittsburgh Sleep Quality Index (PSQI) Hospital Anxiety and Depression Scale Migraine Disability Assessment (MIDAS) questionnaire	Poor sleep quality as measured by the PSQI was significantly associated with a higher total subjective memory complaint ($B = 0.08$, 95% confidence interval [CI] = 0.03-0.14, $p < .01$) and performance on the AD8 ($B = 0.07$, 95% CI = 0.02-0.11, $p < .01$) scores. In addition, more severe depression as measured using BDI was associated with higher total subjective memory complaints and AD8 scores ($B = 0.05$, 95% CI = 0.02-0.09, $p < .01$; $B = 0.08$, 95% CI = 0.05-0.11, $p < .001$ respectively). Subjective cognitive complaints tend to increase with the frequency of migraines with aura and are mediated by depression
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					severity and sleep disturbances.
Chu et al. (2011)	Case Control Cross-sectional	MwPP ($n = 44$) Mw/oPP ($n = 18$) HC ($n = 35$)	MwPP ($36 (\pm 10)$ years) MwoP ($42 (\pm 9)$ years) HC ($37 (\pm 9)$ years)	Photophobia questionnaire Visual discomfort test using three patterns scored (none, mild, mod, sev) visual analog scale	Significant differences were observed in the level of discomfort between groups on each of the conditions ($p < .001$). Median discomfort scores were greater for migraine groups across pattern one ($p < .005$), pattern two ($p < .001$) and pattern three ($p < .001$). Post-hoc analysis revealed migraines with photophobia experience greater more frequent visual discomfort than controls and migraineurs without photophobia.
Ferreira et al. (2018)	Case Control Cross-sectional	CM ($n = 30$) HC ($n = 30$)	Chronic migraine ($33.7 (\pm 11.2)$ years)	Montreal Cognitive Assessment Test, Verbal Fluency Task	Preliminary results from this study found that migraineurs who use topiramate performed significantly poorer than HCs on the verbal fluency task ($p <$

			Controls (33.7 (±9.7) years)	Clock-Drawing Stroop Test Color Trails Test Wechsler Adult Intelligence Scale (WAIS-III): Digit Span (digits forward), Vocabulary, and Matrix Reasoning Rey Auditory Verbal Learning Test 25; Beck's depression and anxiety inventories	.01), Stroop test ($p < .01$), Digit Span ($p < .01$) and Matrix Reasoning ($p < .05$) and MoCA ($p < .01$). Regression analysis controlling for topiramate use, anxiety, depression and poor sleep found that migraine without the use of topiramate, significantly correlated with Verbal Fluency ($p < .01$), Clock Drawing ($p < .01$) and the second and third trials of the Stroop test ($p < .05$). Topiramate use was significantly associated with poorer WAIS-III digit span ($p < .05$) and vocabulary ($p < .05$).
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				Use of Topiramate (drug)	
Gasbarri et al. (2008)	Case Control Cross-sectional	M ($n = 55$) Migraine with Antidepressant Use ($n = 48$) HC ($n = 48$)	Overall ($30 (\pm 3.7)$ years)	Memory task using two conditions: neutral and arousal. Free Recall and Recognition test for each condition.	Female migraineurs performed significantly better at free recall of both arousal ($p < .05$) and neutral ($p < .001$) conditions than male migraineurs. Male HCs performed significantly better recalling the arousal condition than male untreated ($p < .01$) and treated ($p < .01$) migraineurs. In the neutral group, significant differences between the total amount of information recalled was found between the treated migraineurs and healthy subjects ($p < .01$).

					Male HCs had significantly better recognition memory in phase 2 of the arousal condition than both treated ($p < .001$) and untreated ($p < .001$) male migraineurs. Significant differences were further observed between male migraine groups ($p < .001$) Female HCs performed significantly better at the arousal condition than untreated ($p < .005$) and treated migraineurs ($p < 0.005$). In the neutral condition, controls performed significantly better than treated ($p < .001$) and untreated ($p < .001$) migraineurs. Female HCs performed significantly better in phase 2 of the arousal condition than both treated ($p < .001$) and untreated ($p < .01$) female migraineurs. Significant
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					differences were observed between female migraine groups ($p < .001$)
Gil-Gouveia et al. (2015)	Case Control Longitudinal during a spontaneous attack & during an interictal period min 72 hrs after last attack 2 groups for each condition (control for practice effect) no medication or psych/ physio condition	EM ($n = 24$)	EM ($38 (\pm 11.6)$ years)	Zung depression scale State Trait Anxiety Inventory, Symbol search, Trail making A&B, Digit span backwards & forwards, Verbal Fluency, Visual Reproduction, Finger tapping, Famous Faces, Logical Memory, California Verbal Learning Test, Stroop reading, Stroop Colour-Word Test,	Significant differences were observed between base level performance and performance during attack in the following cognitive tests; Stroop word reading ($p < .05$), California Verbal Learning Test (CVLT) total learning ($p < .05$), CVLT short-term recall with ($p < .05$) and without ($p < .05$) semantic help, and delayed recall with ($p < .01$) and without ($p < .05$) semantic help. A significant practice effect was observed for performance on the Stroop word reading ($p < .01$). Similarly, pain intensity during the attack was the significantly associated with performance on CVLT short-term free recall ($p < .01$).

				Snodgrass Naming Test	Supports reversible impairment in learning and memory and language comprehension/attention however perception, motor control and executive function showed no significant difference between ictal states. Many other measures of language function and memory were not significant.
Guo et al. (2019)	Case Control Cross-sectional	M ($n = 46$) HC ($n = 46$)	M (32.84 (± 6.46) years) HC (32.65 (± 6.36) years)	Modified Visual Oddball Paradigm (standard, target and novel stimuli) Self-rating Anxiety Scale, Self-rating Depression Scale,	Using a modified visual oddball paradigm Guo et al. (2019) discovered emotional and interictal attentive processing abnormalities in migraineurs with reduced P3 amplitudes ($p < 0.001$, partial $\eta^2 = 0.125$), P3dT amplitudes ($p < 0.00$, partial $\eta^2 = 0.1871$), P3dN amplitudes ($p < 0.001$, partial $\eta^2 = 0.230$)

				EEG, EOG	and lower P2dN amplitudes ($p < .05$, partial $\eta^2 = 0.070$). Significant effects of gender and group were observed for P3dT ($p < .01$, partial $\eta^2 = 0.095$), P3dN ($p < .01$, partial $\eta^2 = 0.111$) and P2dN ($p < .01$, partial $\eta^2 = 0.089$). Results suggest abnormal visual processing and attention in migraineurs. This impairment is more pronounced in female migraineurs.
Han et al. (2019)	Case Control Cross-sectional	MwoA ($n = 32$) HC ($n = 32$)	MwoA (37.97 (± 8.91) years) HC (39.13 (± 11.38) years)	Attentional networks test (ANT) Mini-Mental State Examination (MMSE), Stroop color-word association test	No significant differences on the MMSE were observed between groups. There were significant effects of group ($p < .00$), flanker ($p < .00$) and condition ($p < .00$) on mean ANT reaction times.

				Shape Trail Test (STT)	MwoA patients exhibited significantly longer response times of the executive control network ($p < .05$), whereas no significant differences were observed in alerting and orienting network reaction times between groups. Migraineurs performed significantly poorer on Stroop III ($t = 2.23, p < .05$) and STT B ($p < .01$) between MwoA and HC groups. Spearman's correlations analysis revealed positive associations between executive control network RTs and both frequency ($p < .05$) and duration ($p < .00$) of migraine attack. Stroop III reaction times were further significantly correlated with migraine duration ($p < .00$) and frequency ($p < .01$).
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					Reaction times for Stroop I ($p < .05$) and II ($p < .05$) and STTB ($p < .05$) were further significantly and positively correlated with attack duration. MwoA patients demonstrate impairments of the executive control network, which appear to be exacerbated by more frequent and longer migraine attacks.
Huang et al. (2017)	Case Control Cross-sectional	M ($n = 34$) HC ($n = 24$)	M (36.07 (± 10.05) years) HC (36.05 (± 12.97) years)	Montreal Cognitive Assessment Rey- Osterrieth Complex Figure Test Digit Symbol Substitution Test EEG/ERP	Overall mean MoCA scores were significantly lower in the migraine group compared to controls ($p < .01$). Significant differences were observed on language ($p < .01$), memory ($p < .01$), executive function ($p < .05$), calculation ($p < .05$) and orientation ($p < .05$) measures of the MoCA. No significant differences on attention and visuospatial measures of the MoCA

					were observed between groups. Migraineurs had a significantly lower score on the memory trial of Rey–Osterrieth complex figure test ($p < .05$). No significant differences were observed on Digit Symbol Substitution and the copy trial of the Rey-Osterrieth Complex Figure Test. No significant difference in accuracy or reaction times was observed between groups. The migraine group displayed significantly longer P3 latencies across parietal ($p < .001$), frontal ($p < .001$) and central ($p < .001$) electrode sites.
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					Migraine duration was significantly correlated with overall MoCA score (-0.478 ($p < .01$)), language (-0.430 ($p < .05$)), executive functions (-0.405 ($p < .05$)), calculation (-0.446 ($p < .01$)) and memory (-0.374 ($p < .05$)). Migraine frequency correlated with scores on the executive functioning (-0.458 ($p < .01$)) and calculation (-0.350 ($p < .05$)) trials of the MoCA and R-OCF recall (-0.415 ($p < .05$)).
Kalaydjian et al. (2007)	Case Control Longitudinal unclear what parameters were used for control group, numerous comorbidities	M ($n = 204$) HC ($n = 1244$)	M ($47.5 (\pm 12.5)$ years) HC ($52.7 (\pm 15.7)$ years)	Mini Mental State Examination (MMSE), Immediate & delayed Recall	Migraineurs from both wave III and IV, had significantly higher mean MMSE values than healthy controls ($p < .05$). Wave IV migraineurs further displayed significantly higher mean immediate ($p < .05$) and delayed ($p < .05$) recall scores

					compared to healthy controls. Migraineurs further displayed significantly lower decline in immediate ($p < .05$) and delayed ($p < .05$) recall over the two waves compared to healthy controls.
Karami et al. (2019)	Case Control Cross-sectional	OLE ($n = 32$) M ($n = 30$) HC ($n = 31$)	Males (25.33 (± 8.24) years) Females (26.08 (± 7.76) years)	Bender- Gestalt II (4 components) Copy - visuomotor ability, perception, visuospatial ability), Recall (visual/ short-term memory), Motor (semantic memory), Perceptual.	Results found significant differences between groups on all components of the BGT-II; copy ($p < .001$), recall ($p < .001$), motor ($p < .001$) and perceptual ($p < .001$) Post hoc examination indicated significant differences between all groups with OLE displaying significant lower copy, recall and perceptual subscores compared to migraine and HC groups ($p < .01$). Migraine followed OLE with lower scores on all components compared to healthy controls ($p < .01$).

Kim et al. (2020)	Case Control Cross-sectional	M ($n = 39$) PPTH ($n = 57$) HC ($n = 39$)	Migraine (41.2 (± 11.5) years) Persistent post- trauma headache (38.2 (± 10.7) years) Healthy Controls (38.3 (9.5) years)	Migraine Disability Assessment Scale (MIDAS) Insomnia Severity index Hyperacusis questionnaire, Allodynia Symptom Checklist, Photosensitivity Assessment Questionnaires, Beck's Depression Inventory, State-Trait Anxiety Inventory,	Insomnia Severity Index scores were significantly higher in the PPTH group followed by migraine and healthy controls ($p < .001$). This trend was further observed with depression and anxiety scores ($p < .001$). No significant differences were observed between groups on the TMT A, TMT B or immediate and delayed recall of the RAVLT between all groups. Significant association with insomnia severity and headache intensity ($p < .05$), Beck's Depression Inventory ($p < .001$) and hyperacusis scores ($p < .05$) in PPTH group. Significant negative association between ISI scores
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				PTSD checklist, Rey Auditory Verbal Learning Test (RAVLT), Trail making test A & B.	and delayed recall in Migraine group ($p < .05$).
Koppen et al. (2017)	Case Control Cross-sectional	MwA ($n = 111$) Mw/oA ($n = 89$) HC ($n = 82$) FHMI ($n = 13$)	MwA (57 (± 8.1) years) Mw/oA (58 (± 7.5) years) HC (55 (± 7.5) years) FHMI (42 (± 13.3) years)	Purdue Pegboard Test, Block-Design Test, Eyeblink Conditioning Task, Body-Sway Test, Wechsler Intelligence Scale, Prism Adaptation Task,	Results found no significant difference between both migraine groups and controls. Slight increase in ischemic lesions in migraine group 8.5% over 4% control group. All lesions (excluding one control) in posterior lobe. Differences in performance between migraineurs with and without posterior lobe lesions were observed. Migraineurs with ischemic lesions displayed significantly lower assembly scores on the

					Purdue-pegboard test ($p < .01$). Participants with FHMI displayed impairment across all primary measures in the study.
Koppen et al. (2011)	Case Control Cross-sectional	M ($n = 16$) HC ($n = 18$) Matched on age, gender, and educational level	M ($58 (\pm 9.1)$ years) HC ($59 (\pm 7.4)$ years)	Global Local Task Attentional Network Task N-back Task	No difference in performance on the Global-Local task, Attentional Network Task, or N-back Task were observed between postictal migraineurs and healthy controls. Migraineurs did not display significant differences in perceptual organisation, working memory and attention during the two-day duration following an attack.
Kriegler et al. (2020)	Case Control Cross-sectional	M ($n = 36$) HC ($n = 38$)	M ($24.75 (\pm 8.61)$ years)	Landmark task (LM), Greyscale task (GRE)	Nonparametric independent samples median test showed differences in greyscale response bias between groups

			HC (25.39 ($\pm$ 8.43) years)		($p < .05$) No difference in landmark task bias was observed. Migraineurs performed similar to that seen in uni-neglect patients on the greyscale task (GRE). The GRE which was significantly impaired in migraineurs requires assessment and attention of luminosity. This impairment is in line with migraineurs being sensitive to high-frequency visual stimuli. Based on GRE task bias, study suggests decreased visuospatial attention in migraine related to decreased activation of temporo-parietal junction.
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Latysheva et al. (2020)	Cross-sectional	CM ($n = 144$) EM ($n = 44$)	CM (42.5 years) EM (37 years)	Perceived Deficits Questionnaire (PDQ), Montreal Cognitive Assessment (MoCA) Digit Symbol Substitution Test (DSST), Rey Auditory Verbal Learning Test (RAVLT), Hospital Anxiety and Depression Scale (HADS)	CM reported greater levels of subjective cognitive deficits as measured by the PDQ ($p < .05$). There was a significant positive association between perceived deficits (PDQ) and HADS anxiety ($p < .05$) and depression ($p < .05$) scores. No significant relationship between PDQ and the other cognitive measures was observed. In the CM group, DSST ($p < .01$) and RAVLT ($p < .01$) scores were significantly lower compared to the EM group. HADS anxiety was significantly and positively correlated with RAVLT ($p < .05$) and MoCA scores ($p < .05$) suggesting anxiety may enhance cognition in migraineurs.
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Lo Buono et al. (2019)	Case Control Cross-sectional	MwA ($n = 50$)	MwA (41.05 (± 14.05) years)	Attentive Matrices	Results showed significant differences between MwA and healthy controls on TMT B ($p < .001$), RAVLT ($p < .01$). Differences between MwA and HC were observed on TMT B ($p < .001$), RAVLT ($p < .001$) and Semantic Verbal Fluency ($p < .05$). In the MwA group significant positive correlations were found between scores on Beck's Depression Inventory and immediate ($p < .01$), delayed memory ($p < .05$), semantic ($p < .05$) and phonemic verbal fluency ($p < .01$) and TMT-B ($p < .01$). In MwA, scores on the Hamilton Rating Scale for anxiety were significantly and positively correlated with
		MwoA ($n = 50$)		Trail Making A (visuomotor + selective attention),	
		HC ($n = 100$)	MwoA (38.29 (± 11.78) years)	Trail Making B, MIDAS,	
			HC (38.16 (± 11.32) years)	Rey Auditory Verbal Learning Test (RAVLT) Semantic and Phonemic Verbal Fluency Beck Depression Inventory Hamilton Rating Scale for anxiety	

					immediate memory ($p < .05$) and TMT-B ($p < .05$). In MwA the Hamilton Rating Scale significantly and positively correlated with delayed memory ($p < .01$) and MIDAS was significantly positively correlated with TMT-B ($p < .01$).
Luedtke & Edlhaime (2021)	Case Control Longitudinal	M ($n = 34$) HC ($n = 4$)	migraine: (42 (± 14) years) control (42 (± 18) years)	Headache diary Personal Health Questionnaire (PHQ-9) Laterality Recognition Task, MIDAS	Migraineurs performed significantly worse in identifying images biased to both left ($p < .05$) and right sides ($p < .01$) than healthy controls. These results were significantly replicated when comparing functioning from pain free days in migraineurs with controls Independent levels of time before, during and after an attack were significantly associated with response times

					to right biased images ($p < .05$).
Martins et al. (2012)	Case Control Cross-sectional	C ($n = 367$) NMH ($n = 50$) M ($n = 61$)	C (66.8 (± 9) years) NMH (69.3 (± 7.9) years) M (61.9 (± 7.6) years)	Mini Mental State Examination, California verbal learning test (CVLT-9) Wechsler Memory Scale III version (WMS-III) Visual reproduction and faces I subtests Trail making test (TMT) Semantic and Phonemic Verbal Fluency	No group differences were found in the majority of cognitive measures. Compared with HC, migraine subjects performed worse on a Symbol Search task ($p < .001$). Non-Migraine Headache (NMH) participants presented more intrusions and worse discriminability in memory recognition and overall lower performance on semantic memory tests.

				Stroop Test Digit Span Symbol Search Wechsler Abbreviated Scale of Intelligence (WASI), Geriatric depression scale (GDS), Subjective Memory Complaints (SMQ)	
Martins et al. (2020)	Case Control Longitudinal	HC ($n = 216$) M ($n = 35$)	WoH: Base: (65.8 (± 8.4) years) Follow: (70.8 (± 8.5) years)	Mini Mental State Examination, Geriatric Depression Scale,	Migraine was not a significant predictor of cognitive impairment at follow-up when controlled for depressive symptoms and age. Results suggest no evidence for increased cognitive

		NMH ($n = 24$)	Migraine: B: (61.1($\pm$7.4) years) F: (66.1 ($\pm$7.3) years) NMH: B: (68.4 ($\pm$6.8) years) F: (73 ($\pm$6.6) years)	Executive function mean: Trail Making Test A + Trail Making Test B + Semantic Food Fluency + Semantic Animals Fluency + Phonemic Fluency Episodic memory mean: logical memory + verbal paired associates MRI: White matter changes and regional cerebral atrophy	impairment risk or steeper cognitive decline in migraineurs compared to HC and NMH groups. Martins et al.(2020) suggest that migraineurs may self-report more specific cognitive complaints.
McKendrick et al. (2006)	Case Control Cross-sectional	M ($n = 29$) HC ($n = 27$).	Median age of both groups was 26 years (range 19–43 for migraineurs, 19–47 for controls).	Global Motion Coherence Thresholds Repeatable Battery for the Assessment of	In the migraine group, mean global motion coherence thresholds were significantly higher than those of controls ($p < .05$).

				Neuropsychological Status (RBANS).	No significant differences were found between migraineurs and controls on the RBANS. Furthermore, performance on the global motion coherence task did not significantly correlate with any of the RBANS index scores. Visual motion perception is impaired in people with migraine when stimuli are presented embedded in noise. No evidence was found for significant interictal cognitive abnormalities in young, otherwise healthy people with migraine. Nor do the data support inattention as an explanation for motion perception abnormalities in migraine.
Messina et al. (2021)	Case Control Cross-sectional	M ($n = 17$)	M (27.7 (range 25 to 46) years)	Angle Discrimination Task,	No differences in reaction time and percentage of correct responses during the angle discrimination task

		HC ($n = 16$)	HC (25.1 (range 24 to 39) years)	Colour Discrimination Task, Trail Making Test, Coding Test, Wisconsin Card Sorting, Line Orientation, Rey Auditory Verbal Learning Test, Rey Osterrieth Complex Figure Test, MIDAS.	were observed between groups. In the colour discrimination task, migraineurs had a significantly reduced percentage of correct scores compared to healthy controls ($p < .05$). No significant differences in reaction times from the colour discrimination task were observed between groups. The comparison of angle vs. colour task revealed an increased activity of the right insula ($p < .05$), bilateral orbitofrontal cortex ($p < .05$) and medial frontal gyrus ($p < .05$), and decreased activity of the bilateral posterior cingulate cortex ($p < .05$) in migraine patients compared to controls. In migraine patients, a better performance in the angle task
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					was associated with higher activation of the right insula ($p < .001$) and orbitofrontal ($p < .001$). Messina et al. (2021) suggest an adaptive functional plasticity that might help migraine patients to overcome impaired visuospatial skills and preserve an adequate performance during a visuospatial task.
Mickleborough et al. (2013)	Case Control Cross-sectional	M ($n = 25$) HC ($n = 25$)	M (26.1 (± 8.7) years) HC (25.8 (± 11.7) years)	Target Identification Task, EEG, EOG	Accuracy or reaction times did not significantly differ between groups. In the migraine group, there was a significant interaction between the task block and both the 200-400 ms and 400-600 ms windows ($p < .001$). In the 200-400 and 400-600 ms time window the increase in block significantly predicted an increase in mean

					amplitude ($p < .001$ and $p < .05$, respectively). Migraine groups may exhibit impaired sensory-level habituation to repetitive evoked visual stimuli.
Miller et al. (2015)	Case Control Cross-sectional	Study 1: M ($n = 9$) HC ($n = 5$) Study 2: HC ($n = 8$) M ($n = 10$) Study 3: HC ($n = 6$) M ($n = 6$)	Study 1: M ($37.4 (\pm 16.1)$ years) C ($33.7 (\pm 14.7)$ years) Study 2: HC ($25 (\pm 6.2)$ years) M ($31 (\pm 9.8)$ years) Study 3: HC ($24 (\pm 2.5)$ years) M ($24 (\pm 4.9)$ years)	Visual Field Movement Task	In the first experiment, post-hoc examination found migraineurs showed increased perception of self-motion recorded by certainty estimations ($p < .05$). In the second trial, using 8s stimuli, the migraine group required significantly greater nulling velocity to cease perception of motion ($p < .05$) The third experiment using longer visual stimuli (16s), found that migraineurs showed significantly increased

					perception of self-motion than controls ($p < .001$). In this task migraineurs further required significantly greater nulling velocity to stop motion perception ($p < .01$).
O'Hare et al. (2018)	Case Control Cross-sectional	M ($n = 15$) HC ($n = 13$)	M (29.27 (± 11.74) years) HC (26.77 (± 7.53) years)	Pattern Glare Test using virtual reality (black skybox) and rilloid patterns.	Migraineurs did not show more tendency for postural sway as no difference was observed between groups. No significant effect of group on illusory motion induced by rilloid pattern was observed.
Öze et al. (2017)	Case Control Cross-sectional	M ($n = 22$) HC ($n = 22$)	Median Age (range) M (42 (20-52) years) C (44 (21-51) years)	Rutgers Acquired Equivalence Task	Mean error ratio and duration of task was significantly greater in migraineurs ($p < .05$, $\eta^2 = .144$). Migraineurs required significantly more trials to complete RAET ($p < .05$, $\eta^2 = .130$). However no significant differences were observed between groups

					when testing acquired pairs of the RAET. In the transfer phase of the RAET, migraineurs performed significantly worse than controls ($p < .001$, $\eta^2 = .288$).
Pellegrino-Baena et al. (2018)	Case Control Cross-sectional	HC ($n = 1227$) NMH ($n = 1742$) MwoA ($n = 804$) MwA ($n = 435$)	HC (55.33 (± 9.4) years) NMH (50.42 (± 8.66) years) MwoA (49.49 (± 7.9) years) MwA (48.13 (± 7.2) years)	Consortium to Establish a Registry for Alzheimer's Disease word list memory test (CERAD-WLMT), Semantic Fluency Test (SFT), Trail Making Test B (TMT-B).	Both MwA and MwoA were associated with poorer cognitive performance on TMT-B $\beta = -0.083$ (95% CI, -0.160; -0.008) and poorer global z-score $\beta = -0.077$ (95% CI, -0.152; -0.002). MwA was significantly associated with poor cognitive performance at TMT-B $\beta = -0.084$ (95% CI, -0.160, -0.008) and global z-score $\beta = -0.077$ (95% CI, -0.152; -0.002). In participants of the ELSA-study, all migraine headaches

					and migraine without aura were significantly and independently associated with poorer cognitive performance.
Poormina et al. (2017)	Case Control Cross-sectional	M ($n = 30$) HC ($n = 30$)	M (28.40 (± 5.29) years) HC (29.30 (± 4.85) years)	Trail Making Test A and B (TMT-A, TMT-B), Stroop Test (colour word)	Compared to controls, migraineurs took more time to complete the Stroop color word test ($p < .001$) and TMT-B ($p < .005$). Among the migraine subjects, obese individuals had an increased frequency of migraine attack per month ($R^2 = .797$).
Puschmann & Sommer (2011)	Case Control Cross-sectional	EM ($n = 17$) FM ($n = 16$) HC ($n = 20$)	EM (41.35 (± 11.87) years) FM (43.4 (± 13.3) years)	MIDAS, State Trait Anxiety Inventory,	No significant difference in STAI was observed between groups however BDI was significantly higher in the FM group.

			HC (39.8 ($\pm$ 10.5) years)	Beck's Depression Inventory, Penn State Worry Questionnaire, Emotional Stroop Index (words and faces).	No significant differences between groups were observed on the word index of the Emotional Stroop. In the face index of the Emotional Stroop, FM displayed significantly less attentional bias to negative stimuli compared to controls and responded quicker to negative faces ($p < .05$).
Quadros et al. (2020)	Cross-sectional	Interictal ($n = 76$) Preictal ($n = 28$) Ictal ($n = 21$) Postictal ($n = 18$)	Total (36.2 ($\pm$ 9.9) years) Interictal (34.7 ($\pm$ 9.7) years) Preictal (38.7 ($\pm$ 8.6) years)	Digit symbol subtest of Wechsler Adult Intelligence Scale III, Trail Making Tests (A, B, and B-A) Stroop Colour Naming.	No significant difference on cognitive measures were observed between ictal states.

			Ictal (37.6 (±10.2) years)		
			Postictal (35.6 (±11.2) years)		
Raimo et al. (2022)	Case Control Cross-sectional	CM (<i>n</i> = 40) HC (<i>n</i> = 40)	Median (range) CM (46 (20-63) years) HC (46 (20-63) years)	The Brief Neuropsychological Examination (ENB-2): Phonemic fluency, Clock Drawing Test, Abstraction, Trail Making (TMT A/B), Cognitive Estimation, Ideative and Ideomotor Praxis Test, Token Test, Digit Span, Immediate and Delayed Recall Prose Memory, Interference Memory at 10 and 30 seconds, Overlapping Figures, Spontaneous Drawing, Copy Drawing	Differences between groups were observed on some neuropsychological measures. The CM group performed significantly poorer than HCs on Overlapping Figures ($p < .0001$), Delayed Recall ($p < .05$), Tower of London ($p < .005$) and the category trial of the Modified Card Sorting Test ($p < .0001$). Significant differences were further observed on Interference Memory at 30 seconds which the CM group performed significantly better than HCs ($p < .01$).

				Modified Card Sorting Test, Tower of London Test. The Italian version of Reading the Mind in the Eyes Task. Modified Italian version of the Emotion Attribution Task, Theory of Mind Picture Sequencing Task, Advanced Test of Theory of Mind (Italian version).	Chronic migraineurs performed significantly poorer than HCs on Emotion Attribution Task ($p < .05$), Advanced Test of Theory of Mind (ATT; $p < .005$) and Theory of Mind Picture Sequencing (TMPS; $p < .05$). Quads rank analysis found significant differences between HC and CM on ATT ($p < .05$), and TMPS ($p < .05$) while accounting for effects of cognitive differences. Poorer performance on Emotion Attribution Task ($p < .05$) and TMPS ($p < .05$) were further significantly associated with the number of headache days.
Ribeiro et al. (2017)	Case Control Cross-sectional	CM ($n = 10$),	CM (35.2 (± 8.4) years)	Iowa Gambling Test,	This shows that there is evidence of alterations in patients with migraine, in the dorsolateral circuit, based on

		Drug Induced Headache (DIH) ($n = 10$), HC ($n = 10$)	DIH (39.6 (± 9.7) years) HC (26.3 (± 1.9) years)	Wisconsin Card Sorting, Trail Making Test, Number/Letter sequence.	neuropsychological tests. The association between migraine and executive disorders can cause a mild cognitive dysfunction. Still patients with migraine from overuse of analgesics showed worse results. A possible impulsivity profile can be highlighted in migraine patients from overuse of analgesics.
Rist et al. (2011)	Prospective cohort study	No Severe Headache ($n = 938$) Non-Migraine Headache ($n = 65$) M ($n = 167$)	No severe headache: (68.9 (± 3.0) years) Non-migraine headache (69.3 (± 3.1) years) Migraine (69.0 (± 2.9) years)	Mini Mental State Examination (MMSE), Digit Symbol Substitution test from the Wechsler Adult Intelligence Scale-Revised, Trail Making Test Part A and B	After adjusting for age, gender, education and smoking status, people with migraine or non-migraine headache did not experience a greater rate of cognitive decline than those without headache or migraine in any domain. For the Wechsler Adult Intelligence Scale-Revised, those with migraine declined less over time ($p < .05$)

				Rey 15-word Memory Test Raven Progressive Matrices, Benton Visual Retention and Facial Recognition Tests, Finger Tapping Test Word Fluency Test 1 minute.	compared to those with no severe headache.
Rist et al. (2012)	Prospective cohort study	Total ($n = 6349$) No history of Migraine ($n = 5496$) MwA ($n = 195$)	At study randomization No history of Migraine ($66.3 (\pm 4.1)$ years)	Baseline questionnaire about migraines. Telephone interview for cognitive status, Immediate and delayed recall trials of the East Boston Memory Test	The global cognitive scores, verbal scores, or telephone interview for cognitive status scores did not differ significantly among the migraine categories. For the category fluency test, the scores differed

		MwoA ($n = 248$)	MwA (65.9 (± 3.9) years)	Delayed recall trial of the telephone interview for cognitive status 10- word list,	significantly among the migraine groups at the second and third cognitive testing ($p <$.05).
		Past history of Migraine ($n =$ 410)	MwoA (65.3 (± 3.6) years)	Category Fluency.	
			Past history of Migraine (66.4 (± 4.13) years)		
			At baseline cognitive interview		
			No history of Migraine (71.9 (± 4.1) years)		
			MwA (71.6 (± 3.9) years)		

			MwoA (71.0 (± 3.5) years)		
			Past history of Migraine (72.1 (± 4.1) years)		
Santangelo et al. (2018)	Case Control Cross-sectional	MwoA ($n = 91$) HC ($n = 84$)	MwoA (33.82 (± 10.53) years) HC (32.27 (± 10.41) years)	Montreal Cognitive Assessment, Beck Depression Inventory-II (BDI-II), Self-version of Apathy Evaluation Scale (AES-S), Italian version of the Memory for Intentions Screening Test (MIST).	Mann-Whitney U test revealed that MwoA performed significantly worse than HCs on each subscale of MIST: time-based ($p < .001$) and event-based scales ($p < .05$), the multiple-choice recognition test ($p < .001$), and 24-h item ($p < .05$). Mann-Whitney U test revealed that MwoA patients made significantly more Task substitution errors than HCs ($p < .005$). No significant difference was found for

					other types of errors.
Santangelo et al. (2016)	Case Control Cross-sectional	MwoA ($n = 72$) HC ($n = 72$)	MwoA : (34.9 (± 11.2) years) HC: (33.8 (± 11.9) years)	Beck depression inventory-II, Self-version of apathy evaluation scale, State-Trait Anxiety, Montreal Cognitive Assessment (MoCA), MIDAS.	Multivariate analysis of variances found significant differences in MCA with migraineurs having lower total MCA ($p < .001$), executive functioning ($p < .005$), visuospatial functioning ($p < .001$) and memory ($p < .001$) compared to HC. However, impairment observed among the MwoA group on MCA was not clinically significant. Correlation analysis found significant negative association between executive function scores and MIDAS ($p < .005$).
Santos-Lasaosa et al. (2013).	Case Control Cross-sectional	CM ($n = 30$) HC ($n = 30$)	CM: (49.33 (± 10.05) years) HC	Mini Mental State Examination (MMSE), Memory Alteration Test,	The CM group showed significantly lower scores when compared to controls for the MoCA ($p < .005$), Memory Alteration Test ($p < .001$) and working memory ($p < .001$).

			(44.83 ($\pm$ 10.91) years)	Montreal Cognitive Assessment (MoCA), Working Memory Task.	No difference was observed between groups on the MMSE.
Schmitz et al. (2008)	Case Control Cross-sectional	M ($n = 24$) HC ($n = 24$)	M (45.50 ($\pm$ 9.31) years) HC (41.50 ($\pm$ 12.90) years)	Go-No Go Task, Motor Stroop Task, SWITCH Task, fMRI	Compared to HC, migraineurs had reduced grey matter in the right middle frontal and left inferior parietal lobes ($p < .05$). Migraineurs showed significantly slower reaction times in SWITCH-effect than controls ($p < .05$). Reaction times to SWITCH-effect in the migraine group were significantly correlated with reduced grey matter density ($p < .05$). No significant difference in performance on the Motor Stroop Task or Go-No Go task was observed between groups

Shepherd, A.J. (2006)	Case Control Cross-sectional	M ($n = 50$) HC ($n = 50$)	Storage I (36 years)	Motion After Effect Task using stationary and dynamic visual stimuli.	No significant differences in motion after effect (MAE) direction was observed between groups.
		Storage I - Grey Screen M ($n = 25$) HC ($n = 25$) Storage II - Eyes Closed M ($n = 25$) HC ($n = 25$)	Storage II (29 years)	Two between factors: group (M and HC) and storage (grey screen or eyes closed) and two within factor conditions: adaption speed slow or fast and storage trial (none or 15s). Motion After Effect (MAE) measured after each trial.	In the migraine group, MAE duration for static stimuli (sMAE) was significantly longer than the HC group ($p < .001$). In the delayed condition, migraineurs displayed significantly greater reduction in sMAE than HCs ($p < .05$). Significant differences between groups were observed with sMAE duration being greater in the migraine group ($p < .05$). For the dynamic visual stimuli, MAE were significantly longer across all conditions in the migraine group ($p < .001$).
Su et al. (2021)	Case Control Cross-sectional	M ($n = 75$)	M (31.87 (± 7.32) years)	Stroop Task,	Migraineurs had significantly longer reaction times in the Stroop Task ($p < .001$)

		C ($n = 41$)	C (31.07 (± 5.61) years)	Mini Mental State Examination, Montreal Cognitive Assessment Test, Hamilton Anxiety/Depression Scale, EEG.	however no significant difference in accuracy or Stroop effect was observed between groups. A significant group effect was found for medial frontal negativity (MFN) amplitude with lower early negative MFN amplitude among the migraine group ($p < .001$). Late MFN amplitude further significantly differed between groups with migraineurs displaying lower negative late MFN amplitude in both congruent and incongruent trials of the Stroop task ($p < .01$). This effect was more pronounced in MwA participants than MwoA or chronic migraine.
Tibber et al. (2014)	Case Control Cross-sectional	M ($n = 22$)	M (34.7 (± 8.3) years)	Visual Acuity,	No significant differences between groups in measures of internal noise (local

		HC ($n = 22$)	C ($34.4 (\pm 6.2)$ years)	Motion Coherence Paradigm, Three Equivalent Noise Paradigms: Size, Orientation and Motion.	processing) and sampling (global processing) across the three paradigms were found. The migraine group had significantly increased motion coherence thresholds compared to the HC group ($p < .05$, Cohen's $d = .78$) ultimately requiring more signal to noise dots to classify the direction of the motion. Tibber et al. (2014) suggest potential impairment in visual noise exclusion in migraine which may be a signature of cortical hyperexcitability.
Tunç et al. (2018)	Case Control Cross-sectional	M ($n = 100$) MwA ($n = 47$) MwoA ($n = 53$)	M ($36.7 (\pm 9.4)$ years) HC: ($34.4 (\pm 11.02)$ years)	Montreal Cognitive Assessment (MoCA), Beck's Depression and Anxiety Inventories,	No significant differences in MoCA scores between the combined migraine group and healthy controls. MoCA scores were significantly lower

		HC ($n = 80$)		Whole-brain MRI.	in MwA compared with MwA and HC groups ($p < .05$ and $p < .05$ respectively). Regression analysis indicated association between MwA and subdomains of MoCA including visuospatial/executive functions ($p < .005$), naming ($p < .05$), memory ($p < .05$), attention ($p < .005$), and abstraction ($p < .005$). Significant negative association with Beck's Anxiety Inventory and MoCA scores. Beck's Depression Inventory was not significantly associated with overall MoCA, however significant associations were found with MoCA subdomains. Significant differences between HC and migraine were found in frequencies of
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					white matter hyperintensities (WMHI) with a significantly larger percentage of migraineurs having WMHI ($p < .05$). Significant association between attack frequency and total MoCA scores was found ($p < .005$).
Viticchi et al. (2017)	Cross-sectional	M ($n = 36$)	M (42.25 (± 10.21) years)	Raven Colour Progressive Matrices	Linear regression underlined a progressive decrease of CPM scores with the increase of the migraine history's length ($R^2 = 0.8871$; $p < .001$) A similar result was obtained for the frequency of migraine attacks ($R^2 = 0.3122$; $p < 0.05$) A pathological CPM can be associated with a longer history of migraine and to a higher frequency of attacks. Accordingly, subjects

					with severe and disabling headaches seem to present an increased probability of developing deficits in reasoning and executive functions. These findings strengthen the hypothesis of the presence of executive functions impairment in MwoA.
Wang et al. (2014)	Case Control Cross-sectional	M ($n = 30$) HC ($n = 30$)	M (33.90 (± 8.81) years) HC (31.63 (± 8.80) years)	Discrimination task: local & global motion perception, McGill Pain Questionnaire, Mini Mental State exam Verbal Fluency,	No significant differences between groups were observed on measures including the MMSE, Beck's Depression Inventory, Digit Span, State Trait Anxiety and Verbal Fluency. In the local biological motion condition, the mean point of subjective equality (PSE) was significantly different between groups ($p < .05$). Unlike migraineurs, the PSE of controls in this

				Beck's Depression Inventory, Digit Span, State Trait Anxiety.	condition was significantly negative ($p < .005$) In the global biological motion condition, PSEs were significantly negative in the migraine and control groups ($p < .05$, $p < .005$ respectively).
Yannick et al. (2015)	Case Control Cross-sectional	M ($n = 45$) HC ($n = 45$)	M (23.29 (± 2.55) years) HC (22.89 (± 2.04) years)	Hospital Anxiety and Depression Questionnaire (HAD), Delis-Kaplan Executive Functions System (D-KEFS) Colour-Word Interference Test.	Migraineurs performed significantly poorer on subtests 1 and 4 of the D-KEFS ($p < .05$ and $p < .05$ respectively). In the migraine group, interference/selective attention scores were significantly lower compared to healthy controls ($p < .05$). In subtests 3 and 4 migraineurs made significantly more errors than the control group ($p < .05$ and $p < .05$) respectively.
Yetkin-Ozden et al. (2015)	Case Control Cross-sectional	M ($n = 74$)	M (37.89 (± 10.99) years)	Short version of the Benton Face	Migraineurs had significantly lower mean LOT ($p < .05$) and

		MwA ($n = 21$) MwoA ($n = 53$) HC ($n = 37$)	MwA (35.33 (± 11.96) years) MwoA (38.91 (± 10.54) years) HC (36.10 (± 11.58) years)	Recognition Test (BFRT), Line Orientation Test (LOT).	BFRT ($p < .05$) scores compared to controls. Differences in mean BFRT were further observed between migraine groups with MwoA performing significantly worse than MwA ($p < .05$).
Zhang et al. (2012)	Case Control Cross-sectional	M ($n = 27$) HC ($n = 27$)	M (33.60 (± 10.41) years) HC (31.96 (± 8.78) years)	Temporal Reproduction Task.	In each case, migraineurs significantly overestimated the duration for the ISI for 1 second ($p < .00$) and for the 5 seconds ISI ($p < .01$). Time estimation for the 600- millisecond condition was impaired in migraineurs in the form of an overestimation.

M = Migraine; C = Controls; EM = Episodic Migraine; CM = Chronic Migraine; MwA = Migraine with Aura; MwoA = Migraine without Aura; HC = Healthy Controls

2.4. Discussion

The goal of the current study was to establish the existence of a domain-specific cognitive profile associated with deficits in individuals suffering from migraine and whether phase specific cognitive impairment existed. The domains reviewed include global cognitive functioning, perception (visual and auditory), attention, memory, visuospatial functioning and executive functioning.

First, for global cognitive functioning, mixed outcomes were observed, depending on measures used. A range of studies using the MoCA showed worse performance in migraineurs compared to controls (Ferreira et al., 2018; Huang et al., 2017; Santangelo et al., 2016, Santos-Lasaosa et al., 2013), one reported an additional mediation of headache frequency (Latysheva et al, 2020) and one pointed to a worse performance for the subgroup of patients with aura (Tunç et al., 2018). Other series of studies using the MMSE showed no differences between migraine patients and healthy controls (Baars et al., 2010; Rist et al., 2011; Wang et al., 2014; Martins et al., 2012, 2020; Santos-Lasaosa et al., 2013), or between episodic and chronic migraineurs (Latysheva et al, 2020), with only a study finding better MMSE scores for migraineurs (Kalaydijan et al., 2007). These contradictory studies point to a problem of accuracy and sensitivity of these cognitive screening tools (Blanco-Campal et al., 2019) and question their relevance in the goal of clarifying the detailed features of cognitive performance in migraine.

In relation to perception, some studies showed an impaired visual perception in migraineurs (Koppen et al., 2011), with more visual discomfort and stress (Chu et al., 2011), and worse left-right discrimination (Luedtke & Edlhaimeb, 2021). When movement is added to what needs to be perceived, performance worsens further

(McKendrick et al., 2006; Shepherd, 2006; Tibber et al., 2014), with an increase in interference (Karami et al., 2019) and illusory motion (Miller et al. 2015), although the latter has been disputed by O'Hare et al. (2018). In terms of auditory perception, two studies (Agessi et al., 2014; Zhang et al., 2012) reported impaired auditory and temporal processing in migraineurs, an impairment whose mechanism needs to be explored further to examine the role of memory and attention on performance.

With regards to attention, studies show quite a consistent pattern of attention and information processing speed deficits in migraineurs (Agessi et al., 2014; Gil-Gouveia et al., 2015; Martins et al., 2012; Mickleborough et al., 2013; Ferreira et al., 2018; Poormina et al., 2017), with some reporting a specific poorer performance in female patients (Guo et al., 2019). Yannick et al. (2015) remark a reduction of selective attention during the interictal period, and Chen et al. (2021) found worse attentional control in migraineurs without aura when compared to health controls. With only one study showing better attention in migraineurs (due to a bias towards faces with negative emotions) (Puschmann & Sommer, 2011), and five studies showing no significant impairment specific to migraineurs (Baschi et al, 2019; Öze et al., 2017; Quadros et al., 2020; Su et al., 2021), overall results point to the need of more research with more accurate measures that take into consideration gender differences, distinction between patient with and without aura, and a focus in determining the specific periods (pre-, ictal, post-, inter-) in which these attention deficits may take place.

In relation to memory, a generalised pattern of decreased memory performance in migraineurs is the main finding across different memory processes (Agessi et al., 2014; Gil-Gouveia et al., 2015; Santangelo et al., 2016; Tunç et al., 2018; Santos-Lasaosa et al., 2013) including general free recall and recognition

(Gasbarri et al., 2008), long-term memory (Raimo et al., 2022), visuospatial memory (Baschi et al., 2019; Huang et al., 2017) and verbal memory tasks (Kim et al., 2020; Latysheva et al., 2019; Lo Buono et al., 2019), independent of aura presence. One study linked migraine to decreased memory performance in a dementia related self-reporting questionnaire (Chu et al., 2020). Separately, a range of studies did not report any significant memory differences between migraineurs and controls (Baars et al., 2020; Kim et al., 2020; Martins et al., 2020; Rist et al., 2011, 2012), with just one of the reported studies finding partial results in favour of migraineurs (Baschi et al., 2019). As with other cognitive domains, measures used to assess memory were very diverse, so the limitations of these neuropsychological measurements need to be considered, as well as the need for a clearly defined protocol of neuropsychological assessment tools.

For visuospatial functioning, results reporting deficits in visuospatial and spatial navigation abilities are scarce and contend with mixed results. Findings from studies, although limited, support the evidence on impaired visuospatial functioning in migraineurs (Karami et al., 2019), with potential implications for high-risk tasks such as, but not limited to, driving, as suggested by Yetkin-Ozden et al. (2015). Messina et al. (2021) showed a significantly decreased performance in migraineurs when compared to controls in relation to spatial navigation tasks requiring colour discrimination (compared to angle discrimination), which seems to indicate the route for further research in this particular domain.

For the domain of executive functions, a general pattern of impaired functions was found across several studies (Huang et al., 2017; Ribeiro et al., 2017; Santangelo et al., 2016; Tunç et al., 2018). In more specific terms, deficits have been reported in migraineurs in terms of slower set shifting and cognitive flexibility (Han

et al., 2019; Lo Buono et al., 2019; Pellegrino-Baena et al., 2018; Poormina et al., 2017; Schmitz et al., 2008; Yannick et al., 2015), impaired decision making (Biagiante et al., 2012; Viticchi et al., 2017), worse performance in working memory tasks (Ferreira et al., 2018; Santos-Lasaosa et al., 2013), and impaired prospective memory (Santangelo et al., 2018). Against this trend, five studies reported non-significant differences between migraineurs and controls (Koppen et al., 2011; Kim et al., 2020; Martins et al., 2020; Quadros et al., 2020; Schmitz et al., 2008), despite some of them showing some trend of a worse performance in preictal stages that requires further research, and only one study (Baschi et al., 2019) reported better significant results for migraineurs. Additional research is required to specifically identify executive function deficits linked to the distinct phases of the migraine cycle.

In conclusion, studies included in this review show mixed and sometimes contradictory findings when it comes to accurately characterising a cognitive profile for individuals with migraine. Overall, visual perception appears to be impaired (and adding movement to perceived stimuli creates further interference and illusory motion) and there is evidence of impairment in auditory and temporal processing, although the precise way in which perceptual deficits affect cognitive performance requires further investigation. Attention is also impaired, as well as memory across different processes (free recall and recognition), stages (specifically, long-term memory) and modalities (visual and verbal). Despite the limited number of studies, visuospatial function and spatial navigation are also affected, and deficits on a wide range of executive functions (set shifting and cognitive flexibility, decision making and reasoning, working memory and prospective memory) complete a complex cognitive profile in migraine.

Consideration should be given to the limitations of the present study is needed. For example, the search syntax used in this study, the search syntax could have been broadened to include terms such as “cognitive” rather than just “cognition” or “visuospatial” rather than “spatial navigation”. As well as this, no measure was taken by the researchers to account for differences in spelling, such as publications using United States spelling conventions.

The development of the current review has faced further obvious limitations derived from the limitations of the existing research. First, in terms of sample selection, many of the reviewed studies included either small sample sizes or non-equivalent group sizes, or both, which may limit the reliability and validity of the results. Moreover, gender or age distribution among the participants was unclear as many studies did not acquire a representative gender or age balance in the migraine groups. In addition, lack of characterization of healthy controls (i.e. absence of clear information about recruitment) was an additional problem. Many studies did not specifically acknowledge whether symptomatology described was linked to a particular migraine stage, although most studies focused mainly on interictal functioning, due to the complexity and sporadic nature of the condition. This limitation impacted the findings of the present review, which was further interested in determining if migraine displayed phase- specific neuropsychological profiles. This however was not possible due to the lack of research accounting for migraine phase. Third, length and chronicity of the condition was not properly addressed in many instances, and studies that examined this found a significant effect of frequency and duration of migraine (i.e. episodic versus chronic migraineurs), making some individuals more vulnerable to cognitive impairment. Fourth, the effect of aura versus non aura was inconsistently reported across the studies

reviewed, and further research is needed to consistently clarify the role of the aura (if any) on the dysfunction across different cognitive domains.

Finally, cognitive assessment protocols were very heterogeneous across studies, and some have relied on very general measures. For example, the use of the MoCA or the MMSE may not be appropriate to evaluate global cognitive dysfunction in migraine. In addition, the validity and reliability of cognitive tests used to specifically assess patients with migraine is another major limitation of the results that has not been properly considered across the studies.

In summary, further research on the cognitive characterization of migraine needs to properly address (1) domain-specific cognitive deficits across different migraine phases (pro-dromal, headache, post-dromal, and interictal); (2) the effects on the length and chronicity of migraine history; (3) the effect of aura versus non-aura (inconsistent across reviewed studies) and (4) the interaction of mood and sleep disorders; as well as other considerations out of the scope of this review, such as gender-specific considerations, effects of different types of medications, potential comorbidities, or differences between primary migraine and migraine due to other underlying medical conditions. As well as this, to reduce heterogeneity of migraine research moving forward, it is recommended that a core outcome set be developed for future research. A core outcome set (COS) is “...an agreed standardised collection of outcomes that should be measured and reported, as a minimum, in all trials for a specific clinical area” (Williamson et al., 2017, p.1). Although a core outcome set for migraine was developed by Haywood et al. (2021), this was developed specifically for preventative intervention trials and may not be applicable to other research designs and aims. For example, it does not include information on attack phase

(prodrome, postdrome) or timing of attacks which may be important in researching the neuropsychological impact of migraine.

But, above all, for a proper characterization of migraine from the neuropsychological point of view, the validity and reliability of the neuropsychological tests used to assess patients with migraine needs to be revisited and the establishment of a clear, consistent and, a cross-culturally applicable cognitive assessment protocol across migraine studies needs to be agreed among the international research and clinical community.

2.5. An update of the literature as of January 2026

The scoping review presented in this chapter (published in 2024), included studies published between January 1st, 2006, to November 30th, 2022. As such, an update of the literature returned under the search syntax was included in the following additional section. This section includes studies published from December 1st, 2022, to January 1st, 2026.

Table 2.2. Summary table of studies included in the review update between December 2022 to January 2026.

Authors and publication year	Study type / Methodology	Participants	Age: Mean (SD)	Measures / techniques used	Summary of main results
Ruiz-Tagle et al. (2024)	Longitudinal, Repeated Measures	Episodic Mw/oA = 14	Episodic Mw/oA (32 years)	Trail Making Tests, Stroop Test, Phonological Verbal Fluency Task, Symbol Digit from the Wechler Adult Intelligence Scale-III, Finger Tapping, N-back task	Neuropsychological task performance was worse during the ictal phase in the TMT A and B. Similarly, there was worse cognitive flexibility and processing speed compared to the interictal phase. However, these differences were not significant. However, only significant differences were observed on Stroop interference ($p = 0.012$) and Finger tap non-dominant ($p = 0.012$). Observed effects are interpreted as being a result of practice in the retest.

				HIT-6, BDI	
Sebrow et al. (2025)	Longitudinal, Repeated measures,	EM = 19	EM (34 years)	Trail Making Tests, Stroop Test, Corsi Block Tapping Task, MIDAS Brief Test of Adult Cognition by Telephone (BTACT)	Significant negative associations were observed on Corsi block tapping. There was significantly less Stroop non-congruent item correct in the interictal phase compared to ictal ($p = 0.006$) and greater Stroop non-congruent errors in the ictal phase ($p = 0.013$) During the ictal phases, there was poorer performance on spatial memory successes/sequences ($p = 0.038$) and spatial memory largest successes/sequences ($p = 0.038$).
Ray et al. (2024)	Prospective Cohort	EM = 16	EM (45.7 (11.5) years)	MSReactor Test Battery: Simple reaction Test, Choice reaction Test, working memory one-back test.	Episodic migraineurs displayed worse working memory, simple reaction time and choice reaction time during the headache and postdrome in comparison to interictal

					baseline. Findings support transient cognitive impairment during the migraine and postdrome phases.
Guo et al. (2024)	Longitudinal, Observational	Episodic MWA = 23 Episodic MwoA = 30 Episodic TTH = 28 HC = 27	MwA (39.15 (8.98) years) MwoA (39.50 (9.54) years) TTH (40.24 (7.83) years) HC (38.15 (10.34) years)	MoCA, Stroop Color and Word Test, Shape Trail Test, Expression related oddball paradigm, GAD-7, PHQ-9, PHQ-15,	Significant differences were found in global cognition ($p < 0.001$) as measured by the MoCA. Significant differences in MoCA subdomains of visuospatial function, executive function, attention and memory ($p < 0.01$) were observed. Combined headache patients performed poorer in MoCA total scores and execution, attention and memory subdomains ($p < 0.03$). No differences between headache groups were observed. Visuospatial function was lower in MwA and MwoA compared with controls ($p < 0.001$).

				EEG	
Lozano-Soto et al. (2023)	Case control, Cross-sectional	CMwoA = 39 HC = 20	CMwoA (45.4 (10.4) years) HC (45.4 (9.6) years)	Symbol Digit Modalities Test (SDMT), Selective Reminding Test (SRT), 10/36 Spatial Recall Test (SPART), Digit Span Forwards & Backwards, Verbal Fluency Tests (Animal Naming Test),	Significant differences between groups were observed on the SRT, DF and Stroop Interference scores with CM patients performing worse during the interictal phase compared to HC. No differences were observed on the remaining tests. Lower disability predicted higher neuropsychological performance.

				Tower of London (TOL), Stroop Color-Word Test, BDI-II, STAI	
Tót et al. (2024)	Case control, Cross-sectional	M = 43 HC = 42	M (34.4 (10.8) years) HC (35.1 (11.3) years)	Sound-Face Test (SFT)	Migraineurs needed significantly less trials to learn associations in the acquisition phase compared to controls ($p = 0.048$). Migraineurs further had lower acquisition error ratios compared to controls ($p = 0.008$). Reaction times were faster for migraineurs than controls in the acquisition phase ($p = 0.048$). No significant differences in retrieval error ratios or reaction times in the test phase.

					Migraineurs displayed better acquisition of audiovisual stimulus pairs in the SFT. These finding contrasts literature using the RAET test.
Monteiro et al. (2025)	Case control, Cross-sectional	M = 40 C = 40	M (33 (5) years) C (35 (4) years)	Stroop Color Test, Addenbrookes Cognitive Examination, Reaction Time Test, Trail Making Tests	No differences in cognitive test scores were observed between groups.
Chowdhury et al. (2024)	Case control, Longitudinal	EM = 122 CM = 28 HC = 150	M (28.9 (8.3) years) HC (28.9 (4.6) years)	Visual Analog Scale, HIT-6, MIDAS,	No difference in MMSE scores were observed between groups. Migraineurs performed worse on Digit Span Backwards ($p < .001$), TMT A & B ($p < .001$), Stroop Word ($p < .001$), Stroop

				Hamilton Depression Rating Scale (HDRS), GAD-7, PHQ-9, MMSE, Digit Span Forward & Backward, TMT A & B, Stroop word, Stroop colour, Stroop Interference	Color ($p < .001$) and Stroop Interference ($p < .05$). Headache variables such as duration, frequency, severity were not associated with test scores.
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Castro Zamparella et al. (2024)	Observational, Cross-sectional	M = 111 EM = 62 CM = 49 Cluster 1 = 74 Cluster 2 = 37	M (38.5 (11.36) years) EM (37.9 (11.1) years) CM (39.2 (11.7) years) Cluster 1 (38.27 (10.9) years) Cluster 2 (38.97 (12.4) years)	HIT-6, MIDAS, Perceived stress scale (PSS), TMT A & B, Verbal Paired Associates Test, Digit Span	No significant differences in cognitive test scores were observed between episodic and chronic migraine patients.
Deodato et al. (2024)	Case control, Cross-sectional	M = 30 HC = 30	M (36 (10) years) HC (29 (14) years)	TMT A & B, Frontal Assessment Battery,	Migraineurs performed significantly worse on TMT ($p = 0.03$) and FAB ($p = 0.001$) compared to the HC group.
Wang et al. (2023)	Case control, Cross-sectional	EMwoA = 51 HC = 45	EMwoA (31.31 (10.03) years)	Computerised Delay Discounting Task, MMSE,	No differences were observed between groups on neuropsychological tests. Migraineurs displayed greater delayed discounting compared to

			HC (31.02 (9.32) years)	Digit Span Forwards & Backwards, Stroop Color Word Interference, Verbal Fluency Test, Hamilton Anxiety Rating Scale, Hamilton Depression Rating Scale	controls ($p = 0.032$) reflecting an impulsive preference for immediate rewards over delayed gratification.
Fathi et al. (2025)	Case control, Cross-sectional	M = n/a HC = n/a	M (31.63 (6.17) years) HC (34.18 (5.21) years)	Addenbrookes Cognitive Examination (ACE-III), Brief visuospatial memory test, Symbol digit modalities test	Significant differences between groups were observed on ACE-III total score ($p = 0.03$). Comparison of ACE-III domains revealed a significantly greater visuospatial scores in the migraine group compared to HC ($p < 0.0001$).
Zengin et al. (2025)	Case control, Cross-sectional	MwA = 8 MwoA = 12 HC = 11	MwA (25.75 (4.39) years) MwoA (28.25 (6.59) years)	Stroop Color and Word	Error rate was significantly higher in the incongruent Stroop task compared to the neutral Stroop in the MwA group ($p = 0.003$).

					MwA displayed significantly greater reaction time interference compared to HC ($p < 0.05$).
Pacho-Hernández et al. (2025)	Case control, Cross-sectional	CM = 70 EM = 70 HC = 70	CM (46.1 (5.2) years) EM (48.1 (7.2) years) HC (49.1 (9.6) years)	Rey-Osterrieth Complex Figure (ROCF), Symbol Search (from WAIS-IV), 5-Digit Test (FDT), Zoo Map Test	Significant differences were observed between groups on Digit Span Sequencing ($p = 0.03$), ROCF recall ($p = 0.02$), ROCF time to copy ($p = 0.03$), FDT decoding ($p = 0.001$), FDT retrieving ($p = 0.001$) and the Zoo Map test ($p = 0.003$). With CM and EM performing worse than HC. Deficits were observed in migraineurs in domains of visual perception, mental inhibition, planning and decision making.

Forkmann et al. (2026)	Case control, Experimental	CM = 59 Chronic back pain (CBP) = 59 HC = 59	CM (38.7 (14.4) years) CBP (43.6 (16.6) years) HC (40 (15.2) years)	Regenburger Word Fluency Test (RWFT), Tests for Attentional Performance (TAP), Trail Making Tests, Verbal learning and memory test, Wechsler Memory Scale Revised	Significant differences between groups were observed on RWFT (fruits-sports) and divided attention measured by TAP ($p = 0.01$ & $p = 0.009$) Post-hoc tests revealed significant differences between HC and CM on RWT with lower scores in the CM group. Post- hoc differences on RWT were further observed between CBP and CM with lower scores in the CM group. Significant difference in TAP was observed between HC and CBP only with worse performance in the CBP group.
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M = Migraine; C = Controls; EM = Episodic Migraine; CM = Chronic Migraine; MwA = Migraine with Aura; MwoA = Migraine without Aura; HC = Healthy Controls

2.5.1. Impressions from the scoping review update

Since completion the scoping review in December 2022, a number of articles exploring neuropsychological functioning in migraine have been published. Of these 15 studies included in the update, 4 were longitudinal designs (Chowdhury et al., 2024; Guo et al., 2024; Ruiz-Tagle et al., 2024; Sebro et al., 2025). The focus on longitudinal studies was a recommendation from the initial review as much of the literature focused on interictal functioning through cross-sectional designs. However, even the updated literature fails to address the potential for prodrome and postdrome cognitive profiles. As such, the research on cognitive functioning in migraine continues to be of limited interpretability. With studies that investigate ictal versus interictal functioning, ictal is limited to the migraine headache. Articles observing impairment, have been initially tested during the headache with repeated testing during the interictal period. As such the difference in cognitive functioning may be interpreted as an effect of first-time exposure to the test with an improvement in the interictal stage being an effect of learning and practice (Ruiz-Tagle et al., 2024; Sebro et al., 2025).

The update to the review further emphasised the persisting lack of consensus on neuropsychological measures used in migraine research, leading to heterogeneous results which are difficult to compare. Furthermore, similar to the initial review, contradictory findings are observed across studies which use the same measures. For example, a number of studies observed significant impairment on the Stroop test compared to controls (Lozano-Soto et al., 2023; Ruiz-Tagle et al. 2024; Sebro et al., 2025); however, no significant differences between groups on the Stroop test were also observed (Wang et al., 2023). Irrespective of these limitations, the updated

literature search further emphasises impaired neuropsychological functioning in migraine and in migraine subgroups across a number of cognitive domains and compels further research in establishing the neuropsychological impact of the disorder.

Chapter Three

Cross-Sectional Associations of Sleep Timing and Eating Behaviour Factors with Migraine in a Predominantly Female Adult Sample.

Richardson, S., Coogan, A. N., & Diaz-Orueta, U. (2026). Cross-sectional associations of sleep timing and eating behaviour factors with migraine in a predominantly female adult sample. *Chronobiology international*, 1–10. Advance online publication. <https://doi.org/10.1080/07420528.2026.2620509>

Abstract

This exploratory study aimed to better ascertain specific features of sleep and eating behaviours associated with migraine. A cross-sectional case-control approach was used with an online convenience sample, 86 individuals with migraine and 74 non-migraine individuals (mean age = 44 y.o.; 90% female), were recruited via social media and university students in Ireland/UK between July 2023 and July 2024. Migraine status was determined by self-report of prior diagnosis by a health-care practitioner; no ICHD-3 interviews were performed. Individuals with migraine showed significantly lower self-regulation ($2.95 \pm .04$ vs $3.17 \pm .09$, $d = .45$), reduced food fussiness ($3.04 \pm .08$ vs. $2.4 \pm .10$, $d = .84$), and increased hunger ($3.30 \pm .08$ vs. $3.00 \pm .08$, $d = -.41$). Both workdays ($7:36\text{h} \pm 0:09\text{h}$ vs. $6:57\text{h} \pm 0:09\text{h}$, $d = -.52$) and weekly average sleep duration ($7:19\text{h} \pm 0:09\text{h}$ vs. $7:44\text{h} \pm 0:08\text{h}$, $d = -0.34$) was significantly longer in individuals with migraine. Non-adjusted logistic regression analysis revealed that longer workday sleep duration ($\text{OR} = 1.69$ (95% CI = 1.12, -2.55), $P = .013$) was associated with increased odds of a migraine diagnosis. While greater self-regulation of eating ($\text{OR} = 0.28$, 95% CI (0.092, 0.88), $P = .028$) and greater food fussiness were associated with reduced odds of a migraine diagnosis ($\text{OR} = 0.29$, 95% CI (0.154, 0.54), $P < .001$). Additional intragroup results for individuals with migraine are also presented. The findings presented in this study suggest a cross-sectional association of migraine with specific sleep and eating factors. However, further research is needed to replicate and expand on the findings observed. Future research availing of longitudinal designs and ecological momentary assessment type measures may shed light on the nature of these factors.

3.1. Introduction

Migraine remains a significant clinical challenge, carrying a high burden for individuals, health care systems and societies; recent estimates of migraine disorder prevalence indicate that 15% of the global population suffers from migraine, which in turn contributes 4.9% of the worldwide total years lost to disability across the lifespan (Abdollahi et al., 2024; Steiner & Stovner, 2023). The adverse impact of migraine emerges not only from the defining feature of unilateral pain but also from various physiological and psychological symptoms that occur in the day preceding (prodrome) and following the headache phase (Karsan & Goadsby, 2018).

Individuals with migraine report changes in a range of behaviours, including, difficulty falling asleep oversleeping or experiencing insufficient sleep, food cravings and increased or decreased appetite (Karsan & Goadsby, 2018; Pavlovic et al., 2014). Impaired sleep and eating habits such as skipping meals or eating certain foods have been linked to triggering migraine attacks (Andress-Rothrock et al., 2010; Mollaoğlu, 2013). However, due to questions regarding the trigger value of sleep disruption and eating behaviours, it has been suggested that such changes may be features of the migraine prodrome (Karsan et al., 2021). This perspective is supported by imaging studies showing increased hypothalamic and limbic system activation, changes that may represent the neural bases of homeostatic behaviour changes, prior to migraine onset (Karsan & Goadsby, 2020; 2023).

Circadian rhythms are recurring patterns in physiological, behavioural and other parameters that recur with periods of approximately 24 hours, and the circadian clock is an important contributor to the timing of the sleep/wake cycle as processes controlled by the circadian pacemaker interact with sleep homeostatic processes

(Borbely, 2022). Similarly, both the timing and composition of meals impact circadian rhythm synchronization, particularly between central and peripheral clocks (BaHammam & Pirzada, 2023). Furthermore, eating behaviours has been shown to impact the sleep cycle by influencing the time of sleep onset and sleep end, with early time-restricted eating causing individuals to go to sleep earlier and wake earlier (BaHammam & Pirzada, 2023; Blum et al, 2023).

The circadian component of migraine has previously been examined, with individuals with migraine reported to be more likely to have extreme chronotype (a preference for earlier or later than sleep timing) and daily patterns in the timing of headache onset (Gori et al., 2005; Sullivan & Martin, 2017; van Oosterhaout et al., 2018). This is not unexpected considering the overlap in neural anatomy important for circadian rhythms, homeostatic and regulatory processes implicated in migraine (Karsan & Goadsby, 2018). It has been suggested that individuals with migraine have greater central responsiveness to environmental stimuli and reduced habituation to repeated stimulus exposure (Abbas Abdulhussein et al., 2022). As such, individuals with migraine are particularly sensitive to environmental changes, including changes to the photic environments, which is of significance as light is the key stimulus for synchronization (entrainment) of circadian rhythms (Artemenko et al., 2021). Furthermore, circadian misalignment has been observed to have significant effects on migraine frequency and severity, while other sleep characteristics such as sleep duration have not, indicating that the link between sleep and migraine is more related to circadian rhythms rather than sleep homeostasis (Benkli et al. 2023; Ong et al., 2018). To date, relatively little research has focused on the relationship between migraine and sleep timing and consistency, circadian rhythms and eating habits and preferences with migraine. To address this knowledge

gap, the current study aimed to examine the associations of sleep timing and eating habits in individuals with migraine in comparison to individuals without migraine.

3.2. Methods

3.2.1. Participants

Non-random convenience sampling was used to recruit a sample of 160 participants (86 individuals with migraine and 74 age-matched individuals without migraine; see Figure 3.1). Recruitment took place from 19/06/2023 to 9/06/2024. The inclusion criteria for this study were: participants must be at least 18 years of age; individuals with migraine were required to have been diagnosed with primary migraine disorder by a licensed healthcare practitioner. However, the survey acquired self-reported data on migraine diagnosis by a licensed healthcare provider using a binary yes or no response. Exclusion criteria were based on self-reported data, participants were required to have no diagnoses of a sleep disorder or other major chronic physical or psychological conditions (excluding migraine). The use of self-report migraine diagnosis reflects research that highlights the reliance of Irish and British migraine populations on general practitioner diagnosis and care due to lack of access to specialist neurological care (Vaghi et al., 2023). The lack of access is demonstrated by studies by Darcy et al. (2023) which estimates less than 1 neurologist to 100,000 of the population in Ireland with no research on Irish and British general practitioner approaches to diagnosis. However, it is outlined by the Health Service Executive (2025) that diagnosis should be made in line with the International Headache Classification of Headache Disorders (3rd edition). Similarly, while there are some screening measures for migraine diagnosis, none of these are

comparable to a clinical diagnostic evaluation completed by a specialist, which is not accessible to many patients (Vaghi et al., 2023).

The link to join the study voluntarily and to complete the study survey was inserted in the study information sheet. The study link was shared by different means, including via the first author's work and personal social media accounts, and targeted distribution to online community groups across Ireland and the United Kingdom. The Migraine Association of Ireland posted the link to the survey on their organization's social media, mailing list and website. This study was also made available to undergraduate students to participate as part of Maynooth University's Department of Psychology research participation scheme, where students receive academic module credits for their participation.

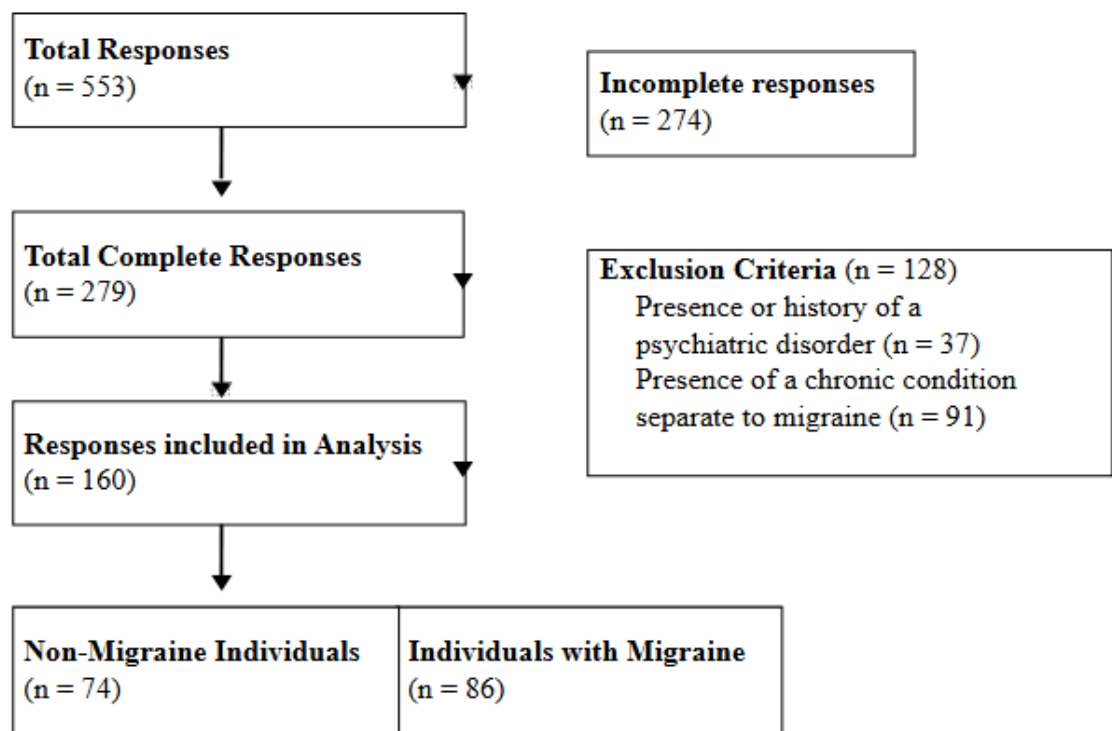


Figure 3.1. Flow chart showing total survey responses, total complete response and total responses included in the final analysis following exclusion of individuals who answered “yes” to having a history of psychiatric disorder or presence of a chronic condition excluding migraine. Participants who were missing small amounts of data were included in the final analysis (n = 9).

3.2.2. Procedure

An online survey of approximately 20-25 minutes for completion was circulated to participants, and all responses were anonymized at the point of collection. The survey included demographic and other bespoke items using Likert scales on how regular sleep and eating habits were, the times at which participants typically eat and sleep, and questions on migraine severity and frequency. Standardized questionnaires used were the Munich Chronotype Questionnaire (MCTQ; Roenneberg et al., 2003), the single-item Sleep Quality Scale (Snyder et al.,

2018), the Sleep Regularity Questionnaire (Dzierzewski et al., 2021), the Adult Eating Behaviors Questionnaire (Hunot et al., 2016), and the Self-Regulation of Eating Questionnaire (Kliemann et al., 2016). The *Munich Chronotype Questionnaire* (MCTQ) assesses individual chronotype (conceived as the phase of circadian entrainment) using the time of sleep corrected midsleep on “free” days (details of scoring in Roenneberg et al., 2012). The difference between midsleep on free days and workdays was calculated as an absolute value of Social Jetlag, indicating the misalignment between social and biological rhythms. Similarly, using the MCTQ data weekly sleep loss was also calculated (details in Roenneberg et al., 2012). The MCTQ has been validated against sleep-log recorded sleep timing over a 5-week period (Roenneberg et al., 2003). This validation analysis observed significant correlations between the MCTQ, and sleep-log recorded timings, with regression slopes close to 1 suggesting very strong criterion validity (Roenneberg et al., 2003).

The single-item Sleep Quality Scale (SQS) consists of an 11-point Likert Scale and asks participants to consider their overall sleep quality over the past 7 days. The scale ranges from 0 to 10 with 0 being terrible and 10 being excellent (Synder et al., 2018). The scale has demonstrated good test-retest reliability at 1-week (intraclass correlation coefficients [ICC] = .74) and at 7-weeks (ICC = .55) (Synder et al., 2018). The SQS further displayed good convergent validity with sleep measures such as the Pittsburgh Sleep Quality Index (Pearsons $R = -.72$) (Synder et al., 2018). The SQS further displayed ability to measure clinically meaningful differences in sleep quality with 2-to-3-point increase or decrease indicating greatly worsened and greatly improved, respectively, and a 1 point increase or decrease further indicated somewhat worsened and somewhat improved, respectively (Synder

et al., 2018). The *Sleep Regularity Questionnaire* (SRQ) is a 6-item questionnaire aimed at assessing circadian regularity and sleep continuity (Dzierzewski et al., 2021); participants answer questions using a five-point ordinal scale with responses including not at all, a little bit, somewhat, moderately and very much. Lower scores on this measure suggested more irregular sleep patterns (Dzierzewski et al., 2021). Initial psychometric examination of the SRQ indicated good test-retest reliability (ICC = .71 to .83) and moderate construct validity with the Pittsburgh Sleep Quality Index ($r = -.37$) and the Insomnia Severity Index ($r = -.39$). The *Adult Eating Behaviours Questionnaire* is a 35-item questionnaire that assesses individuals eating behaviour on eight factors: enjoyment of food, emotional overeating, emotional undereating, food fussiness, food responsiveness, slowness in eating, hunger and satiety responsiveness (Hunot et al., 2016). The questions are answered using a five-point ordinal scale with 1 being "Strongly Disagree" and 5 being "Strongly Agree". Each factor is assessed individually, with higher scores indicating greater expression of the factor. Each of the eight factors demonstrated good internal consistency (Cronbach's $\alpha = 0.75 - 0.90$) and test-retest reliability (ICC = 0.73 – 0.91; Hunot et al., 2016). Furthermore, expected associations with each factor were observed; for example, food avoidance traits were negatively associated with body mass index (BMI) while food approach traits were positively associated with BMI (Hunot et al., 2016). Due to an error, the questions on emotional undereating were not included in the data collection process and therefore the emotional undereating factor scores were not calculated for this study (Hunot et al., 2016). The *Self-Regulation of Eating Behaviours Questionnaire* (SRBEQ) comprises eight questions, three of which are screening questions aimed at establishing whether participants generally try to maintain a healthy diet and what unhealthy foods may be tempting, while the

remaining five questions focus on individual eating intentions and ability to avoid tempting foods using a five-point ordinal scale (never, rarely, sometimes, often, always; Kliemann et al., 2016). Higher scores on the SREBQ suggest greater self-regulation of eating behaviours. Psychometric examination revealed good internal consistency (Cronbach's $\alpha = 0.75$) and good test-retest reliability (ICC = 0.77). Furthermore, the questionnaire indicated good concurrent validity with regulatory scales such as the Perceived Self-Regulatory Success in Dieting Scale and Self-Control Scale (Kliemann et al., 2016) and as good convergent validity with dietary habits such as fruit and vegetable consumption, sweet and salty snack consumption as well as physiological measures of BMI (Kliemann et al., 2016). Finally, the SREBQ demonstrated good discriminant validity against measures such as food fussiness, satiety responsiveness and slowness in eating (Kliemann et al., 2016). All measures used in this study can be found in Appendix A.

3.2.3. Data Analysis

Independent samples T-tests were used to examine groupwise differences between migraine and individuals without migraine on parametric dependent variables, and Mann-Whitney-U tests were used for groupwise comparisons on the non-normally distributed dependent variables of absolute social jetlag and weekly sleep loss. One-way analysis of variance was used to examine normally distributed sleep and eating variables between groups of migraine frequency (less than one attack per month, up to 14 migraine days per month and over 15 days per month) and Kruskal-Wallis non-parametric tests were used to examine differences in social jetlag and weekly sleep loss. All missing values were excluded on a case-wise basis. Binary logistic regression was used to estimate the associations of the predictor

variables identified from the groupwise comparisons with the binary probability of migraine diagnosis (migraine versus non-migraine); the predictor variables included were sleep duration on workdays, total self-regulation of eating behaviours, food fussiness and hunger. Weekly sleep duration was not included in the model due to high collinearity with sleep duration on workdays. Missing data were coded for, and as per SPSS 26 default for logistic regression analysis; participants with any missing data from the included variables were excluded. Similarly, the data was screened for extreme outliers and multicollinearity among the variables.

This study approach was quasi-exploratory; whilst it has been established that significant relationships may exist between migraine and homeostatic behaviours such as sleep and eating, specific relationships between circadian rhythms have returned mixed results and little research has examined the regulation of such behaviours between groups. For this reason, specific *a priori* hypotheses for this study were not formed. Due to the exploratory nature of this study, corrections for multiple comparisons were not applied to the following analyses. The significance value was set to $p < 0.05$, and Cohen's *d* indicated effect sizes as interpreted according to Cohen (1988). Sensitivity analysis was further conducted for results which were significant in the main analysis for added interpretability of the findings. For the sensitivity analysis, sleep duration on workdays, the weekly average sleep duration, average self-regulation of eating, average food fussiness, and average hunger were recoded into categorical ordinal variables. The weekly sleep duration and workday sleep duration variables included the levels < 5 hours, 5-7 hours, $> 7 \leq 10$ hours and > 10 hours. The significant eating behaviour variables, mean self-regulation of eating, mean food-fussiness, and mean hunger were transformed to include the levels low (1- 2.5), moderate (2.6- 3.5) and high (3.6 - 5).

Independent Samples T-Tests were then used to assess groupwise differences between individuals with and without migraine. This study has been made available on the Open Science Framework website accessible through the following link: https://osf.io/enjym/?view_only=cff0d17328194e1890f774e7eb4140c5.

3. 3. Results

Table 3.1. Descriptives table of sample characteristics. Means and standard error of the mean alongside group frequency, number and percentage are presented as appropriate. * Indicates groupwise difference $P < 0.05$.

Variable	Non-migraine	Migraine
	Mean (SE) / N (%)	Mean (SE) / N (%)
Age (years)	43.92 (1.19)	44.10 (1.11)
Sex		
Female	64 (87%)	82 (95%) *
Male	10 (14%)	3 (4%)
Employment status		
Unemployed/ Retired (%)	11 (15%)	11 (12.8%)
Employed Part-time	18 (24%)	14 (16%)
Employed Fulltime	40 (54%)	54 (63%)
Student	5 (7%)	6 (7%)
Workdays per week.	4.83 (.15)	4.66 (.15)
Migraines		
> 1 per month		23 (27%)
1 – 14 per month		47 (55%)
≥ 15		16 (18%)
Migraine Pain Severity		
Mild		3 (4%)
Moderate		38 (44%)
Severe		45 (52%)
Migraine Duration		
< One day		39 (45%)
> One day		39 (45%)

Analysis of the sample descriptive statistics revealed that both groups were sufficiently age-matched (mean age of the migraine group = 44.10 years, range = 18 – 69 years; non-migraine group = 43.92 years, range = 25 – 65 years; $p = .987$; Table 3.1). Both groups were predominantly female, with 95% of the migraine group being female and 87% of the non-migraine group. The breakdown of sex in the experimental and control group was statistically different ($p = .028$ between groups). In the migraine group, the majority of participants had episodic migraine, ranging from 1 to 14 migraine days per month (55%); infrequent migraine (less than 1 migraine day per month) followed this with chronic migraine (15 or more migraine days per month) being the least frequent in the migraine group at 18% (see Table 3.1). Before regression analysis, all variables were assessed for multicollinearity (See Figure 3.2).

Group-wise comparison revealed no significant differences between individuals with migraine and individuals without migraine on MSFsc, SJL, and subjective sleep quality (Table 3.2 and Figure 3.3). Significant differences in sleep duration were observed, with individuals with migraine having significantly longer sleep duration on work days ($7:36\text{h} \pm 0:09\text{h}$) compared individuals without migraine ($6:57\text{h} \pm 0:09\text{h}$, $d = -.52$) Significant differences in average nightly sleep duration across the full week was also observed: in comparison to individuals without migraine ($7:19\text{h} \pm 0:09\text{h}$), individuals with migraine had significantly greater weekly sleep duration ($7:44\text{h} \pm 0:08\text{h}$; $t(142) = -2.07$, $p = .041$, $d = -0.34$; Table 3.2 and Figure 3.3).

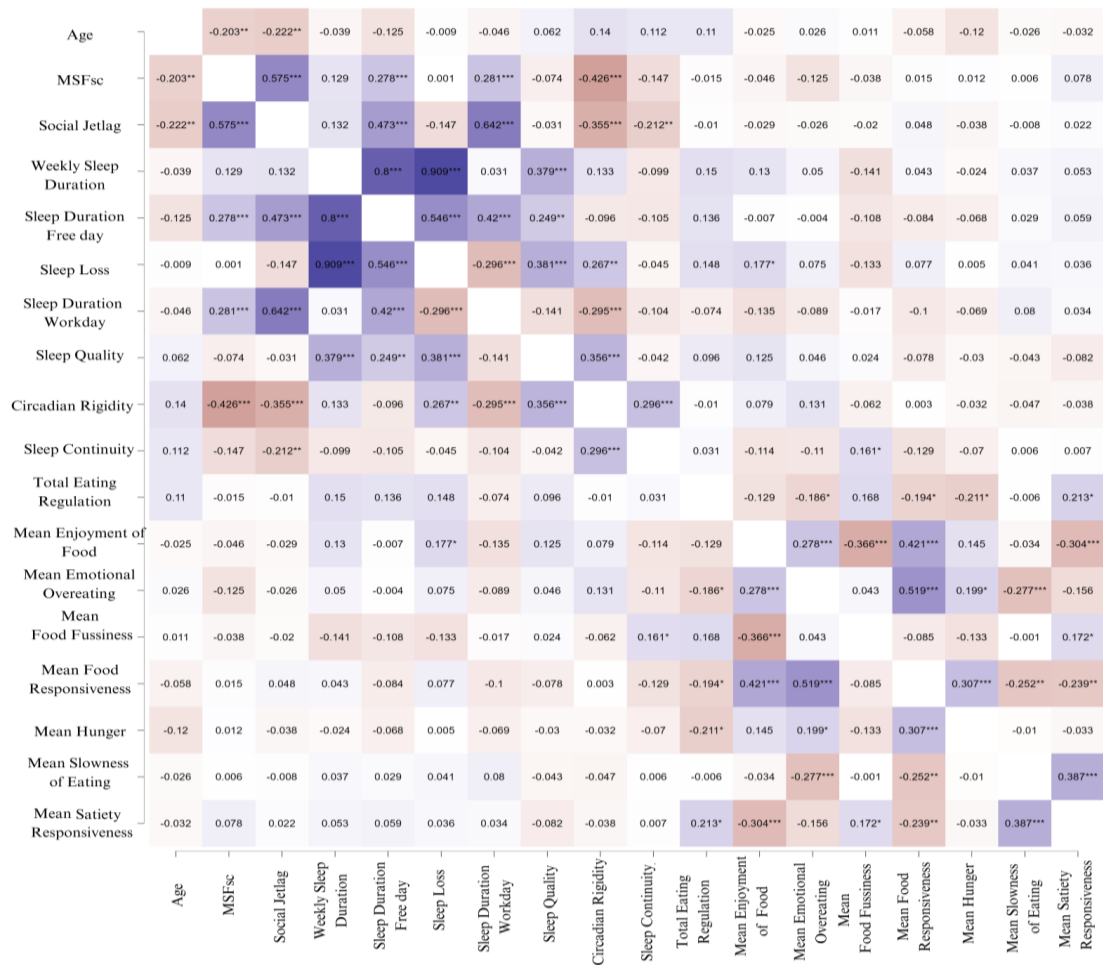


Figure 3.2. Correlational heatmap of all the sleep and eating variables included in this study across the entire sample (individuals with and without migraine). Shades of red indicate negative associations while purple shades indicate positive associations. Significant correlations (Pearsons R) are denoted with asterisks.

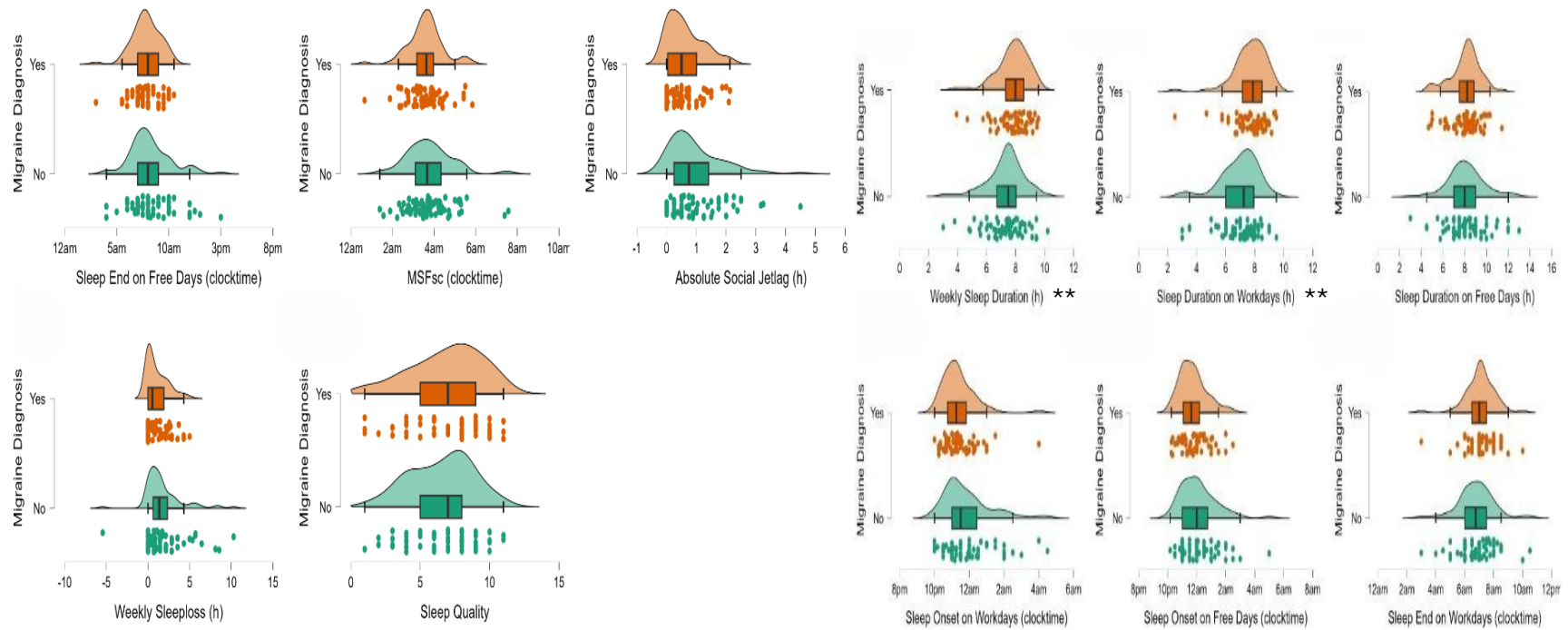


Figure 3.3. Raincloud plots highlighting distribution of sleep variables (Weekly Sleep Duration, Midsleep on Freedays, MSFsc, Sleep Loss, Absolute Social Jetlag and Sleep Quality) between migraineurs (yes) and non-migraineurs (no).

Table 3.2. Groupwise comparisons of sleep variables between individuals with migraine and individuals without migraine.

	Non-Migraine				Migraine				<i>P</i>
	<i>N</i>	<i>Mean</i>	<i>Median</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>Median</i>	<i>SE</i>	
MSFsc (hh:mm)	74	03:48	03:44	0:08	86	03:48	03:51	0:06	.80
Sleep Duration (h:m)	72	07:19	07:30	0:09	72	07:44	07:56	0:08	.041
Sleep Loss (h:m)	74	1:46	1:22	0:16	72	1:07	0:42	0:09	.134
Social Jetlag (h:m)	74	0:57	0:45	0:06	86	0:43	0:30	0:05	.428
Sleep Quality Workdays	74	6.49	7.00	.263	76	6.66	7.00	.304	.67
Sleep Onset (hh:mm)	74	23:51	23:30	0:08	86	23:33	23:20	0:07	.11
Sleep End (hh:mm)	74	06:49	06:53	0:08	86	07:02	7:00	0:07	.18
Sleep Duration (h:m)	72	06:57	07:15	0:09	72	07:36	07:48	0:09	.002
<u>Free days</u>									
Sleep Onset (hh:mm)	74	00:07	24:00	0:08	86	23:58	23:45	0:06	.41
Sleep End (hh:mm)	74	08:16	08:00	0:14	86	07:58	08:00	0:09	.27
Sleep Duration (h:m)	72	8:09	8:00	0:12	72	8:03	8:12	0:09	.72

Table 3.3. Groupwise analysis of sleep regularity and eating regulator variables.

	Non-Migraine			Migraine			<i>p</i>
	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	
Circadian Rigidity	74	15.47	.36	86	15.98	.34	.311
Sleep Continuity	74	6.43	.25	86	6.78	.23	.316
Self-Regulation of Eating	55	3.17	.09	66	2.06	.04	.022
Food Enjoyment	70	3.91	.09	86	4.08	.08	.181
Emotional Overeating	70	2.87	.12	85	2.92	.10	.777
Food Responsiveness	69	2.91	.08	84	2.97	.09	.612
Slowness in Eating	70	2.85	.11	83	2.66	.06	.358
Satiety Responsiveness	68	2.77	.09	85	2.76	.09	.924
Food Fussiness	70	3.05	.10	85	2.36	.11	< .001
Hunger	70	3.00	.08	83	3.28	.08	.014

Analysis of variance examining sleep variables (MSFsc, sleep duration on workdays and self-rated sleep quality) and regularity variables (circadian rigidity and sleep continuity) between migraine frequency groups returned no significant differences across all variables, and non-parametric groupwise analysis returned no significant differences in median weekly sleep loss values and social jetlag (Table 3.4). Finally, analysis of variance examining eating behaviours using variables from the AEBQ and SREBQ (food enjoyment, emotional overeating, food responsiveness, slowness in eating, satiety responsiveness, food fussiness, hunger and self-regulation of eating) between migraine frequency groups returned significant differences for levels of food fussiness $f(2, 83) = 4.32, p = .016$ (Table 3.5). Due to unequal group sizes, Bonferroni post hoc examination for multiple comparisons was used to

determine the differences among the groups. Post hoc examination revealed that mean food fussiness was significantly lower in the < 1 per month migraine frequency group ($11.90 \pm .16$, $p = .014$) in comparison to the 1-14 per month frequency group ($2.56 \pm .14$).

Table 3.4. Comparison of sleep and regulatory variables across migraine frequency groups.

Migraine Frequency per month	<1			1 - 14			≥ 15			<i>P</i>
	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	
MSFsc (hh:mm)	23	03:53	0:10	47	03:50	0:09	16	03:52	0:14	.99
Social Jetlag (h:m)	23	0:42	0:10	47	0:49	0:07	16	0:49	0:09	.36
Sleep Loss (h:m)	22	1:08	0:15	37	1:06	0:13	13	1:04	0:25	.96
Workday Sleep Duration (h:m)	22	7:43	0:12	37	7:24	0:13	13	7:58	0:21	.30
Sleep Quality	23	7.57	.456	47	6.60	.393	16	5.38	.931	.06
Circadian Rigidity	23	16.65	.550	47	15.58	.520	16	16.19	.593	.39
Sleep Continuity	23	6.04	.447	47	6.81	.294	16	7.75	.588	.05

Table 3.5. Comparison of Adult Eating Behaviours Questionnaire variables and Self-Regulation of Eating across migraine frequency groups.

Migraine Frequency per month	<1			1 - 14			≥ 15			<i>p</i>
	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	
Mean Food Enjoyment	23	4.30	.14	47	3.94	.12	16	4.15	.19	.17 1
Mean Emotional Overeating	23	3.04	.20	46	2.93	.14	16	2.71	.19	.54 5
Mean Food Responsiveness	23	2.89	.18	46	2.95	.11	15	3.15	.20	.59 1
Mean Hunger	23	3.13	.16	45	3.31	.11	15	3.39	.16	.50 0
Mean Satiety Responsiveness	23	2.47	.16	47	2.92	.11	15	2.70	.29	.11 1
Mean Food Fussiness	23	1.90	.16	47	2.56	.14	15	2.44	.25	.01 6
Mean Slowness of Eating	22	2.59	.23	46	2.66	.15	15	2.75	.28	.90 0
Total Self- Regulation of Eating	15	3.04	.07	40	2.94	.05	11	2.91	.09	.45 5

Binary logistic regression was used to regress on presence of migraine diagnosis to assess a model with four predictor variables that were significantly different in the previous analysis between migraine groups (sleep duration on workdays, self-regulation of eating, food fussiness and hunger; Table 6). The model was statistically significant, (χ^2 (4, N= 106) = 36.86, $p < .001$) and explained between 30.5% (Cox & Snell) and 30.7% (Nagelkerke) of the variance in the dependent variable migraine diagnosis. The model's predictive value was good and

correctly classified 73.6% of participants. Sleep duration on workdays significantly and independently increased the odds of being an individual with migraine (OR=.1.69 (95% CI=1.12, -2.55), $p=.013$). Of the eating behaviour variables, greater eating regulation was significantly associated with reduced odds of a migraine diagnosis (OR = 0.28, 95% CI (0.092, 0.88), $p = .028$). Similarly, higher food fussiness was also associated with significantly lower odds of having a migraine diagnosis (OR = 0.29, 95% CI (0.154, 0.54), $p < .001$).

Table 3.6. Results of binary logistic regression with migraine diagnosis as the dependent variable.

Variable	B	SE	Wald	df	<i>p</i>	Odds Ratio	95.0% C.I.	
Sleep Duration (Work)	.68	.208	10.80	1	.013	1.69	1.12	2.55
Eating Regulation	-1.26	.572	4.82	1	.028	.28	.092	.88
Food Fussiness	-1.24	.32	14.85	1	.001	.29	.154	.544
Hunger	.32	.374	.74	1	.427	1.38	.664	2.86

Groupwise comparison of the categorical sleep variables for sensitivity analysis revealed significant differences in workday sleep duration with individuals with migraine having significantly longer sleep duration than individuals without migraine (2.69 vs. 2.47 respectively; $t(140.6) = -2.31$, $p = .011$, $d = -.39$) with an effect size comparable to the original analysis. However, using the categorical variable for weekly sleep duration, no significant differences were observed between individuals with and without migraine (2.76 vs. 2.64, respectively) (Table 3.7).

For the eating behaviour variables, significant differences were observed between individuals with migraine and individuals without migraine on levels of categorical mean hunger (2.27 vs. 1.91) with individuals with migraine displaying significantly higher levels of hunger $t(151) = -3.14, p = .001, d = -.51$. Significant differences were further observed for levels of categorical mean food fussiness between individuals with migraine and individuals without migraine. Results from the groupwise comparison revealed significantly reduced levels of food fussiness in individuals with migraine compared to individuals without migraine (1.54 vs. 1.99; $t(152.7) = 4.22, p = .001, d = .67$). No significant differences in categorical levels of mean self-regulation of eating were observed between individuals with migraine and individuals without migraine (2.05 vs. 2.11, respectively) (Table 3.7).

Table 3.7. Results of groupwise comparisons of transformed categorical variables of sleep duration (work and weekly average), average self-regulation of eating, average food fussiness, and average hunger.

	Non-Migraine			Migraine			<i>p</i>
	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	
Sleep Duration (week)	72	2.63	.07	72	2.76	.06	.089
Sleep Duration (work)	72	2.47	.07	72	2.69	.06	.011
Self-Regulation of Eating	55	2.11	.08	66	2.05	.03	.244
Food Fussiness	70	1.99	.08	85	1.54	.08	< .001
Hunger	70	1.91	.08	83	2.27	.08	.001

3.4. Discussion

This study explored sleep timing and quality and eating behaviours in individuals with migraine compared to individuals without migraine. We do not report significant differences on the circadian variables of MSFsc and social jetlag between the migraine and non-migraine groups. Previous studies have found that individuals with migraine report earlier diurnal preference when compared to individuals without migraine, using the Morning-Eveningness Questionnaire to assess preferred timing of sleep/wake behaviours (Sullivan & Martin, 2016). A study by Baska et al. (2025), found that the odds of being an evening chronotype were significantly greater in individuals with migraine compared to controls. However, the MCTQ provides measures of actual sleep timing behaviours rather than the psychological preference assessed by the MEQ, and use of MCTQ-derived measures such as MSFsc have been reported to show no significant between groups differences between those with and without migraine disorder in sleep timing (Horne & Östberg, 1976; van Oosterhout et al., 2018). Further, Ong et al. (2018) reported significant difference in midsleep as measured by actigraphy between individuals with migraine and individuals without migraine. Im Yun and Chu (2019) have reported that individuals with migraine who experience a time pattern of migraine attack onset had significantly earlier MSFsc than individuals with migraine whose attacks followed no time pattern. Given this, it is possible that no significant difference in MSFsc was observed between groups of individuals with migraine and individuals without migraine in the current study as typical time-of-day of migraine attacks were not assessed. We also report no differences in social jetlag according to migraine status; as we report no difference between individuals with migraine and individuals without migraine in MSFsc and social factors such as employment status,

the finding of no difference in social jetlag may not be surprising given the emergence of social jetlag as an interaction between chronotype and social schedules such as working time (Roenneberg et al, 2019).

No significant differences in sleep regularity variables of circadian rigidity or sleep continuity were observed, nor were there groupwise differences in these variables between migraine frequency subgroups. These findings are consistent with our findings of no differences in sleep timing measures (sleep onset, offset or midsleep on both work and free days, social jetlag), and further suggest that habitual sleep/wake timing is not altered in migraine disorder relative to matched controls. Future work might usefully confirm these findings work by comparing longitudinal actigraphy measurements or other objective measures of sleep with the Sleep Regularity Questionnaire while keeping in mind that individuals with migraine may try to counteract perceived aggravating factors or triggers related to sleep such as under or over- sleeping (Agbetou & Adoukonou, 2022; Sullivan et al., 2022; Turner & Houle, 2018). Interestingly, no differences in sleep quality were observed between individuals with migraine and controls or within migraine frequency groups. Research on sleep quality using the Pittsburgh Sleep Quality Index has observed significant associations between sleep quality and migraine diagnosis (Kouhi Fayegh et al., 2023). As such, it is worth noting that in this study sleep quality and sleep continuity were close to significance which may represent a type II error and may explain incongruencies between the findings from this study and the literature. Such contrasting findings may further be explained by sampling bias or measurement differences.

Individuals with migraines slept significantly longer than individuals without migraine on workdays and also had significantly longer average nightly sleep

duration by nearly half an hour compared to non-migraine individuals. Sensitivity analysis using transformed categorical variables observed significant differences in sleep on workdays suggesting a more robust effect of workday sleep over the weekly average. Longer sleep duration may be indicative of the imperative of achieving sufficient sleep as a means to avoid ‘triggering’ a migraine attack (Sullivan et al., 2022). In the current study, individuals with migraines worked fewer days per week than individuals without migraines, although this difference was very small and not statistically significant. Although the literature suggests that migraine can impact on employment due to the unpredictable and debilitating nature of the condition (Raggi et al., 2012), it does not appear to be likely that differences in employment status underpin differences in other factors between people with and without migraine in the current sample.

Differences were observed in eating regularity, with individuals with migraine displaying lower self-regulation of eating behaviours, lower food fussiness, and greater hunger when compared to individuals without migraine. Sensitivity analysis using transformed categorical variables for the significant eating behaviour variables further supported the reliability of reduced food fussiness and greater hunger in individuals with migraine. Further caution may be taken regarding the robustness of overall self-regulation of eating which was not significant in this analysis and further investigation into this variable is required for future studies. Similarly, analysis of variance within migraine frequency groups found significant differences in mean levels of food fussiness. Food fussiness was lowest for individuals with < 1 migraine per month in comparison to individuals with 1-14 migraines per month. Hunger and total eating regulation were negatively associated with each other, however food fussiness was not associated with either variable;

therefore, it does not appear likely that reduced food fussiness is driven by increased hunger (See Figure 3.2). No differences were observed between migraine frequency sub-groups on mean levels of eating behaviours including food enjoyment, emotional overeating, food responsiveness, hunger, satiety responsiveness, slowness of eating and self-regulation of eating, suggesting no relationship between these eating behaviours and migraine frequency. Significant differences were observed between individuals with < 1 migraine per month and individuals with 1- 14 migraines per month on levels of food fussiness. Food fussiness was lower in individuals with infrequent migraine occurring >1 month when compared to individuals with episodic migraine (1-14 attacks per month). Further investigation in future studies may examine the relationship between migraine frequency and self-regulation of eating behaviours with larger and equal sized frequency subgroups as well as incorporating information on typical time of migraine onset.

It was predicted that sleep and eating variables would be associated with each other in this study due to both being intrinsic markers of and regulators of biological rhythms (BaHammam & Pirzada, 2023; Blum et al, 2023). However, few significant associations were observed between sleep and eating variables in this study. Food fussiness was significantly and positively associated with sleep continuity, and food enjoyment was significantly and positively associated with weekly sleep loss while no differences in circadian variables were observed. No other associations between sleep and eating variables were observed. It would seem that for the most part the eating and sleep variables included in this study are independent of each other. The relationship between circadian variables and eating may further be regarding the timing of eating rather than behavioural qualities assessed in this study (BaHammam & Pirzada, 2023; Blum et al, 2023).

This study aimed to investigate differences between groups of sleep and eating regulation between individuals with migraine and individuals without migraine to address gaps in existing literature. With respect to the theoretical frameworks employed in this thesis, the present study highlighted the role of hypothalamic-based behaviours in migraine such as sleep and eating behaviours (Giffin et al., 2003; May & Burstein, 2019; Schulte & May 2016). However, it is not possible to determine whether differences in sleep duration and eating behaviours between individuals with migraine and non-migraine controls can be interpreted as dysfunction in migraine, nor can the clinical significance of the differences be inferred from the present study. Interestingly, no differences in circadian variables of chronotype (MSFsc) or circadian misalignment (social jetlag) were observed. It is possible that differences in circadian regulation are transient and occur in relation to migraine occurrence, and as such may not have been detected via a cross-sectional design. Future research using longitudinal approaches to assess functioning across different phases of the migraine cycle (interictal, prodrome, headache and postdrome) is required to clarify and expand on the relationship between migraine and circadian rhythms. Taken together, these findings provide further insight into the relationship between migraine and hypothalamic-regulated behaviours, while highlighting the complexity of researching sporadic conditions such as migraine.

An important strength of the current study is the use of a number of instruments to examine different aspects of sleep/wake timing and eating behaviours in migraine to allow for possible delineation of specific sub-domain effects. This study also has a number of important weaknesses, including the limited sample size of the groups included in this study overall and particularly within migraine frequency subgroups. Furthermore, the breakdown of gender in the sample was not

representative with a notable lack of male participants in both groups although slightly worse in the migraine group. This limits the generalizability of the findings, and the study should be interpreted within the context of a predominantly female sample. Another limitation to this study is the reliance on self-report measures of health status including migraine diagnosis and history or presence of psychiatric and physiological chronic health disorders, which impacts the reliability of the findings. It is possible that the migraine group includes individuals that have been incorrectly diagnosed with migraine. In the same regard, participants in this study may have undiagnosed health conditions which may have confounding effects on the findings. Similarly, this study lacked demographic and clinical information on racial/ethnic identification, education, income and socio-economic status, body mass index, caffeine intake, alcohol intake and tobacco use which further limit the generalizability and reliability of the findings. Socioeconomic status, education and income bracket has diverse impacts on health behaviours relevant to this study including eating and sleeping, as such it is not possible to account for the effects of these demographic variables (Darmon & Drewnowski, 2008; Giskes et al., 2010; Grandner et al., 2010; Patel et al., 2010).

It is also important to reflect on the limitations of the sampling methods used. Firstly, no a priori power analysis was conducted to determine the sample size required for the analyses included in this study. Given the number of analyses undertaken it is likely that the present study was underpowered and the results should be interpreted with caution (Button et al., 2013). As well as this, convenience sampling via online migraine groups and followers of the Irish Migraine Association would not have been representative of Irish and British populations, and by design excluded individuals who lacked the necessary access to technology. In the same

regard, online migraine groups would have targeted a subset of individuals with migraine who were seeking online support and information regarding their migraines and potentially overlooked those who did not access these online support groups. As such, the sample may not be representative and potentially skewed.

While consideration was taken to preserve the statistical power of the study, replication is necessary to evaluate the reliability of these results. The use of standardized self-report measures in this study may not completely represent individual behaviours accurately and there is a lack of psychometric information on the performance of the measures in individuals with migraine. As such, there is a need for studies availing of more objective and longitudinal recordings. We did not elicit information on the use of migraine medication, and such treatments could influence sleep and eating behaviours. The decision to not include medication usage in this study was due to the limited power of the study coupled with the many medications which are available to both individuals with migraine and non-migraine participants. It was also not feasible to recruit individuals with migraine who were not using pharmacological treatments for the condition. For this reason, it is important that future studies aim to replicate the associations of sleep and eating behaviours observed in this study while controlling confounding demographic and clinical variables that are overlooked in this study. Finally, while sleep and eating behaviours were mostly not associated with each other in this study, future studies examining the timing of meals and their nutritional composition in relation to sleep in individuals with migraine and individuals without migraine may be more informative (BaHammam & Pirzada, 2023). Similarly, future studies may consider a design which may discern whether any causal relationships between sleep and eating factors exist in migraine pathology to examine whether changes in sleep are

contributing factors or consequential to migraine. Alongside this, there is a need to examine diet and eating behaviour in migraines using more robust measures such as food and migraine diaries with careful consideration of clinical and demographic confounding factors. If the findings of the present study are replicable, the clinical value of sleep and eating factors in migraine management should be investigated further.

3.4. Conclusion

The results of the current study provide evidence for only modest associations of migraine disorder with sleep habits and eating behaviours. Of note, sleep duration on workdays, total self-regulation of eating and food fussiness emerged as the factors most strongly associated with migraine and warrant further investigation.

Chapter Four

Understanding the Lived Experience of Migraine in Irish Adult Females: A Qualitative Study.

Abstract

This study aimed to explore the lived experience of migraine in a sample of females living in Ireland. The complex nature of migraine and its multifaceted impact is one which is often overlooked in positivist approaches to understanding disability. Furthermore, research on the migraine experience of Irish females is limited. In this study, 10 adult females participated in online semi-structured interviews. A data driven, reflexive thematic analysis was used to formulate themes that expressed the participants' experience of migraine. Results from the study highlighted four overarching themes in the data: *Mental Wellbeing*, *It's Not Just a Headache*, *Treatment: Trial and Error*, and *Fight for Control*. The theme of *Mental Wellbeing* highlighted the nuanced and bidirectional relationship between migraine and mental health emphasising experience of anxiety and shame arising from living with migraine, a fluctuating experience of resilience or lack thereof. The theme *It's Not Just a Headache* portrayed the presentation of migraine as a complex nervous system disorder, composed of a multitude of symptoms and importantly, how this is rarely acknowledged. The theme *Treatment: Trial and Error* depicted the nature of migraine treatment as an experimental process and the participants experience of public and private care in Ireland. The theme *Fight for Control* further captured the experience of the participants in trying to manage the condition and limit the impact and disability of migraine; contrasted by the inevitable loss of control, where migraine is unresponsive to attempts of prevention and treatment. This study highlights the significant impact of migraine among Irish females, demonstrating the importance of recognising migraine-related disability and adopting a functional approach to care within Irish public and private health services, emphasising the bio-psycho-social dimensions of the condition.

4.1. Introduction

The global burden of disease study estimates that for every 100,000 of the population in the Republic of Ireland, 25% suffer from migraine (23,000 < 25,000 per 100,000) (Stovner et al., 2018). However, this is likely an underestimate of the true frequency due to lack of patient awareness and frequent misdiagnosis due to reliance on tertiary non-specialist care (Viana et al., 2019). Migraine is also three times more prevalent in females in comparison to males with incidence peaking in adolescents and young adults (Fan et al., 2023; Lebedeva, 2022). The impact of migraine goes beyond the distinguishing feature of pulsing headache but also consists of a wide range of symptoms and impairments which are physiological, affective, sensory, and cognitive (Richardson and Diaz, 2024; Rosignoli et al., 2022). These symptoms are less frequently discussed in the literature and less well-known to the general population (Rosignoli et al., 2022; Karsan & Goadsby, 2021). Therefore, there is a lack of awareness around the severity of migraine impairment, which contributes to a lack of understanding and stigma (Young et al., 2013).

As with any chronic or long-term illness, the impact of migraine is greater than the exhaustive list of symptoms and includes a more nuanced impact on the lived experience of the individual. Research on migraine has found a significant social impact on relationships such as those closest to the individual, including immediate family, spouses and children (Buse et al., 2016). The impact of migraine in the workplace is frequently noted as increased absenteeism (Lofland and Frick, 2006). However, more recent studies highlight the dimensional nature of the impact in the workplace, such as increased weekly work duration, presenteeism and frequency of occupational burnout among migraineurs in comparison to non-

migraineurs (Peles et al., 2023; Shimizu et al., 2021). Migraine has been reported to negatively impact quality of life, with people with migraine displaying higher than normal levels of anxiety and depression (Antonaci et al., 2011; Domitrz and Golicki, 2022; Duan et al., 2023). Findings such as these, however, are often reductionist in nature, limiting the impact of migraine to standardised measures and definitions without capturing the lived experience of migraine. Despite the significant frequency of migraine in Ireland, the Irish migraine population remains under-represented in migraine research and even more so in qualitative research that aims to understand the subjective lived experience of migraine, which is often overlooked and simplified by positivist quantitative designs (Stovner et al., 2018). Capturing the lived experience of migraine in Ireland is particularly important given evidence that, due to limited access to specialist services, most individuals with migraine in Ireland are diagnosed and managed within general healthcare settings (Vaghi et al., 2023). Furthermore, research suggest the disability and impact of migraine was greatest for women aged between 15 and 49 years (Stovner et al., 2018). Studies investigating specialist and non-specialist care in migraine has further highlighted differences in approaches to treatment with greater proportions of patients in specialist settings receiving migraine specific acute and preventative medication in comparison to those treated by general practitioners (Katsarava et al., 2018). Furthermore, research has observed sex disparities in pain treatment with health care professionals dismissing the severity of female pain (Guzikevits et al., 2024). Research on migraine has been approached qualitatively and highlights the complex psychosocial impact of migraine such as approaches to coping beyond medication and the impact on social and work functioning and relationships (Dione et al., 2024; Nichols et al., 2017). A recent study by Flynn et al. (2024) investigates migraine experiences among a

sample of Irish university students however such findings may not be representative to individuals with migraine outside a university setting. As such, this study aims to portray the lived experience of migraine in an Irish sample of females diagnosed with primary migraine as a step to increase awareness and improve treatment of migraine in the Republic of Ireland. The present study will also investigate the subjective experience of the migraine prodrome and postdrome, to see if this aligns with the measures used to capture phase-specific impairment, and the relevant findings of such in the quantitative chapters presented alongside this study. Furthermore, when considered alongside the quantitative chapters in this thesis, it is hoped this qualitative study will enable a truly comprehensive understanding of the lived experience of migraine.

4.2. Methods

4.2.1. Participants

Ten individuals with migraine were voluntarily recruited to participate in this study. The sample size was decided with relation to the limited participant pool as such no specific considerations of saturation were considered. Due to the broad nature of the study, which is not theoretically driven, a larger sample would have been preferred although unattainable for the present study (Malterud et al., 2016). Participants who were interested in taking part in the longitudinal study described in Chapter Five, were asked to email the researcher expressing interest in participation. All individuals were screened regarding the inclusion criteria. If eligible, participants were asked to provide their home address to post out study materials for the longitudinal study alongside information and consent sheets which had to be signed and returned by post to the researcher. The information and consent sheets included details of both the longitudinal study and the qualitative study outlined here and in

Chapter Six. It was hoped that using one sample of participants for both studies would enable a comprehensive understanding of their migraine and enable critical feedback on their experience participating in the previous longitudinal study. Following completion of the longitudinal study, participants were emailed and asked if they would still like to take part in semi-structured interviews that aimed to capture the subjective experience of migraine that was not considered in the longitudinal study. The inclusion criteria for participating were the same as those of the longitudinal study (see Chapter Five) and included the following: (1) individuals were required to be at least 18 years old and able to provide informed consent; (2) they had to have daily access to the internet; (3) a professional diagnosis of primary migraine was required, with neither a secondary health condition that may be causing their migraine, nor a history of psychiatric treatment and diagnosis. Moreover, due to the nature of the previous study it was also required that (4) participants were a resident of the Republic of Ireland. The ten participants who took part in the study were all female with ages ranging from 32 to 63 years, with the mean age being 43 years. Of these participants, six were diagnosed with migraine without aura and four were diagnosed with migraine with aura, two of whom occasionally experienced migraine without aura. For the purpose of the analysis, participants were given numbers to maintain anonymity (Participant 1, Participant 2 ... Participant 10). Names of specific locations and medications were removed from the interviews. Participants were initially informed about this study alongside the longitudinal study

4.2.2. Data Collection

All participants were provided with an information sheet detailing the study information, requirements and participants' rights prior to participating. Included in

this, contact information for Samaritans and Migraine Association of Ireland were provided should participants need to avail of support following participation (See Appendix C). All participants were asked for informed consent before participating, which included consent to record the audio of each interview to enable transcription (See Appendix D). Interviews were conducted online using Microsoft Teams between December 2023 and May 2024. A semi-structured interview format was used to enable focus on key topics that centred around different levels of migraine impact, such as the individual level, work and social domains (See Table 4.1). Some questions were also included to understand the potential impact of migraine before and after a migraine occurs, that is, to understand the prodrome and postdrome phases proposed by recent research. However, this schedule was not exhaustive, and participants were encouraged to add any information that they thought might be important and might have been overlooked by the study. Interviews lasted approximately one hour; however, this varied greatly from participant to participant. The audio from each interview was recorded and automatically transcribed using Microsoft Teams. The researcher then listened to each interview with reference to the draft transcript to ensure accuracy. An orthographic transcription method was used to generate a detailed verbatim account of each interview, including both speech and non-verbal vocalizations. This study was approved by the Social Research Ethics Subcommittee at Maynooth University.

Table 4.1. Schedule used for the semi-structured interviews with participants.

1. How long have you been experiencing migraines?
2. Has your experience with migraine changed over time?
3. How often do you experience migraines now?
4. Has the frequency of your migraines or how often you experience them changed over time?
5. Do you know when you are going to get a migraine before the pain begins? How?
6. Do you ever notice changes in how you are feeling both physically and mentally in the days before an attack? Can you please explain.
7. Do you experience changes in your ability to perform tasks? What kind of tasks? When would you experience this change?
8. How does migraine impact your mood?
9. Do you have any other symptoms that happen before you experience migraine pain?
10. How does migraine impact your wellbeing?
11. Do migraines impact your work?
12. Do migraines impact your social life?
13. What about more personal relationships?
14. Is there anything about your experience of migraines I may have missed that you would like to talk about?

4.2.3. Data Analysis

The data were then analysed using an experiential approach to reflexive thematic analysis as outlined by Braun and Clarke (2006; 2019). Thematic analysis was selected as it is a flexible analytic approach in qualitative research and is suitable for the data and aims of the study which is to portray the lived experience of migraine in an Irish sample. Thematic analysis was also suitable as it enables accessible sharing of qualitative findings to non-expert readers, such as individuals with migraine, who may wish to access this research. An experiential approach was primarily used to fulfil the aim of the study, which was to describe the participants' understanding of their experiences living with migraine. The approach used in this study was mostly inductive and driven by the content of the interviews. However, some theoretical frameworks did shape the analysis, such as existing disciplinary knowledge on the high comorbidity of anxiety and mood disorders in the condition and presence of psychological, behavioural and physiological symptoms secondary to the migraine headache (Antonaci et al., 2011; Domitrz & Golicki, 2022; Duan et al., 2023; Karsan & Goadsby, 2021). Furthermore, the primary researcher is diagnosed with migraine and has lived experience of the condition.

The approach acknowledges the active role of the researcher in creating understanding and generating themes from the data. As the participants had previously taken part in a separate longitudinal study that lasted a minimum of three months, there was a relationship between the researcher and the participants before the interviews. On reflection, this seemed to enable the participants to be more comfortable in sharing their personal experiences and their vulnerabilities. Similarly, it was known by the participants that the researcher had migraines too, and as such, a sense of the researcher as being particularly understanding of their experiences was

conveyed by the participants. However, it has to be noted that the mode of the interviews being online Microsoft Teams calls would have had some effect on the participants' likelihood of sharing more intimate information as opposed to a data collection method that the participant completes alone, without the social interaction with the researcher.

The analytic procedure began as outline by Braun and Clarke (2006; 2019) with the familiarisation of the interview data. During this stage, the researcher read the transcripts and made notes of key points of interest, such as recurring topics. In this stage, it was also important to consider the meaning behind the data (Braun & Clarke, 2006; 2019). Each interview was read in full a minimum of two times during the familiarisation stage. Following the familiarisation stage, the researcher began reading through each of the transcripts and identifying segments that were relevant to the research question or of particular interest. The qualitative software MAXQDA was used to accumulate and keep track of recurring codes in the transcripts. This approach to coding is best described as *complete coding*, as the approach was more general and open than, for example, selective coding, which has very clearly defined topics of interest (Braun & Clarke, 2006; 2019). Codes were written to be concise and capture the important information and interpretation of the data. Some segments of the data included multiple codes. When each interview had been coded, the codes were revised and considered with regards to the interview segments they captured and whether codes were linked to each other and could be grouped together to depict a more nuanced theme or pattern in the data. Once themes had been developed, it was necessary to review the coded segments and ensure that the themes accurately reflected the coded data. Once themes were finalised, they were written up with reference to segments from interview transcripts to illustrate the experience of the

participants. This analytic process was not linear, and each step was revisited multiple times, with various proposed codes and themes discarded or edited throughout the writing process.

4.3. Results

Of the ten participants in the study, six had migraine without aura and four had migraines with aura with occasional attacks without aura. Many of the participants had been diagnosed with migraine for a significant amount of time ($M = 25.7$ years, $SD = 11.31$ years; (see table 4.2)). The mean age of the participants was 45 years ($SD = 11.25$ years). Two of the participants had retired early from their careers due to migraine while the rest of the sample maintained part-time or full-time employment. The final iteration of the analytic process produced four overarching themes to data: *mental well-being*, *it's not just a headache*, *treatment: trial and error and fight for control* (see Table 4.3 & Figure 4.1). The theme *mental well-being* had three subthemes: *anxiety*, *self-conscious emotions* and *resilience*. The theme *treatment: trial and error* had three subthemes: *can't rely on medication*, *trial and succeed: the benefits of medication and lack of professional knowledge*. The theme *fight for control* had two subthemes: *try to control: I have to keep going*, and *loss of control*. The theme *it's not just a headache*, had two subthemes: *the prodrome and the postdrome*, and *social perception*.

Table 4.2. Demographic information of the participants, including participant identification numbers, sex, age (years), migraine employment status and self-report duration of diagnosis.

Participant Identification	Sex	Age (years)	Migraine Type	Employment Status	Diagnosis Duration
1	Female	46	MwoA	Part-time student/ part-time employed	6 years
2	Female	63	MwoA	Employed part-time	40 years
3	Female	36	MwoA	Employed full-time	21 years
4	Female	32	MwoA	Employed full-time	17 years
5	Female	33	MwA	Employed full-time	12 years
6	Female	45	MwoA	Employed full-time	32 years
7	Female	63	MwA	Employed part-time	30 years
8	Female	37	MwA	Retired	27 years
9	Female	49	MwA	Employed full-time	37 years
10	Female	49	MwoA	Retired	35 years

Note. MwA = Migraine with aura, MwoA = Migraine without aura

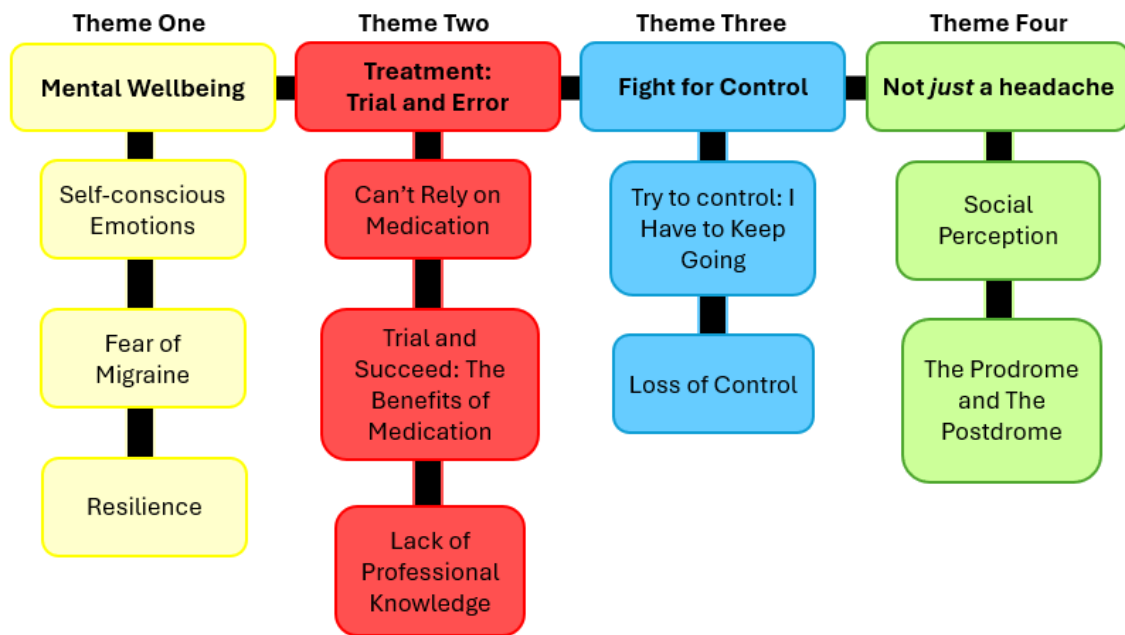


Figure 4.1. Thematic map of the themes presented in the results of this study.



Figure 4.2. Document portraits of the coded interviews displaying the frequency of codes throughout each interview, with the top five portraits displaying interviews from participants 1- 5 from left to right and the bottom five portraits of participants 6-10 from left to right. Green squares represent coded segments from the theme of More Than Just a Headache. Red squares are segments coded in the theme of Treatment: Trial and Error, Blue squares are segments coded in the theme Fight for Control, yellow squares are segments coded in the theme Mental Wellbeing.

Table 4.3. Table outlining the themes and subthemes that were included in the final analysis, with subsequent descriptions of the subtheme and included codes.

Theme	Subtheme	Description
Mental Wellbeing	Fear of migraine	This subtheme describes the expression of fear and anxiety by participants in relation to general and situational migraine attack occurrence. This subtheme includes the codes “anxiety” and “avoidance”.
Mental Wellbeing	Self-conscious emotions	This subtheme describes self-conscious emotions expressed by participants as they reflect on themselves in relation to personal and social values. This includes the codes “guilt” and “shame”.
Mental Wellbeing	Resilience	This subtheme relates to information on the expression of acceptance of participants’ individual circumstances and helpful perspectives.
Treatment: Trial and Error	Can’t rely on medication	This subtheme describes participants’ experience with medication. This includes the subcodes, “Rationing the medication”, “Medication not working” and “Coping during the attack”.
Treatment: Trial and Error	Trial and succeed: The benefits of medication	This subtheme covers any benefits associated with medication, such as greater normality.
Treatment: Trial and Error	Lack of professional knowledge	This subtheme captures the overall lack of professional knowledge in migraine due to the subjective nature of migraine. This includes the codes “Self-directed care” and “Disappointed and disheartened”.
Fight for Control	Try to control: I Have to Keep Going	This subtheme encapsulates the need to try to control the migraine. This includes behavioural strategies to try and prevent an attack and preparation to manage the attack and the circumstances around the attack. This includes two codes: “Try to prevent” and “Prepare for an attack”.
Fight for Control	Loss of Control	This subtheme encapsulates the loss of control when an attack occurs. This includes the codes “Impacting on daily tasks” and “Loss of time”.
It’s not <i>just</i> a headache	Social Perception	This subtheme captures the social perception of migraine by the

		participants' peers. This subtheme is dichotomous in that it mostly included the negative codes “lack of understanding” expressed by others and the “strain on relationships”; but there were also positive codes such as “understanding” and “help from peers”, which captured the compassion and recognition of others.
It's not <i>just</i> a headache	The Prodrome and The Postdrome	This subtheme captures all prodrome and postdrome symptoms of the participants prior to and following the cessation of migraine pain. This includes the codes “prodromal autonomic symptoms”, “prodromal affective symptoms”, “prodromal physiological symptoms”, “prodromal cognitive symptoms”, “postdrome cognitive symptoms” and “postdrome affective symptoms”.

To maintain the readability of the chapter, the most representative topics and quotes have been presented below. Additional details and extracts of participants' answers on each theme and subtheme are presented in Appendix B.

4.3.1. Theme One: *Mental Wellbeing* ($n = 9$)

Throughout the interviews, participants ($n = 9$) referred to mental-health difficulties they experienced as a result of having migraines. Such difficulties included anxiety around having a migraine attack, which often led to avoidance behaviours. This anxiety around having a migraine attack is discussed under the subtheme ‘fear of migraine’. As well as anxiety, participants expressed negative emotions, guilt and shame due to a discrepancy between their perceived self and their values, often referring to what is expected of them by others and themselves. These negative appraisals of the self and consequent emotions are described under the subtheme ‘self-conscious emotions: guilt and shame’. The toll of migraine, both

mentally and physically, on the participants was evident, and participants spoke of how easily this can take over, and the need to actively resist the negative impact emerged in the subtheme ‘resilience’.

4.3.1.1. Subtheme One: Fear of migraine (n = 7)

The nature of migraine as a sporadic and difficult-to-treat condition with frequent unresponsiveness to pharmacological interventions can have a significant impact on mental well-being. In this study, one way that migraine was described as impacting mental well-being was by creating excessive anxiety around the anticipation of a migraine attack and the situational perceived ability to cope. Participants often spoke of “what if” situations centred around a migraine occurring at random and inconvenient times. The unpredictable nature ultimately means that at times, a migraine attack will interfere with responsibilities and commitments that require participants to be present and able. For some participants, this was associated with a degree of overthinking and anxiety. A situation of being stuck in the crack between abled and disabled, making the appraisal of what one can commit to difficult. This ultimately was a trigger for stress and anxiety.

Both in work and outside work, of just the worry of if I commit to doing that, what if I can't do it? And you know, opportunities that come up and I go, “oh, gosh, yeah, I could do that” ... but what if I get a migraine and I can't actually do it on the day? (Participant 9)

Alongside migraine, creating stress and anxiety around trying to manage the responsibilities and expectations associated with life, some participants expressed anxiety around the severity of some particularly debilitating migraine attacks. The thought of these severe attacks occurring where there is a lack of support, for

example, at work or outside the home, was particularly worrying. For one participant, this anxiety was evoked every time they had to leave the house to go to work, emphasising the difficult nature of being temporarily disabled.

You know you're anxious as in, is it going to develop, what am I supposed to do? You know that kind of way. I kind of keep thinking about it, worrying, you know, worrying about is it going to develop into something so bad and how am I going to get home 'cause I'm not going to be able to drive.

(Participant 7)

Some participants expressed a more general level of anxiety and fear of migraine instigated by the anticipation of an attack, regardless of the setting and based more so on the infliction of the attack itself.

(when an attack occurs) "I am feeling some anxiety because I know it's coming." (Participant 10)

"...it's if you get any hint of a symptom like nausea, pain in my temple. I put my head in my hands, and I say, "oh God, oh, God, oh God. What's that now...?" (Participant 7)

This fear of the migraine precipitated hypervigilant behaviour to try to prevent the attack onset or a worsening of the attack. For example, one participant mentioned they are *"always conscious if I do too much physically, you know, particularly with moving my head up and down and things like that, I'm going to bring this migraine on more"* (Participant 10)

Due to this fear and anxiety associated with migraine, individuals expressed a level of avoidance, particularly around specific events and activities, fearing they

would trigger a migraine. To the participants who spoke about such occasions, the nature of these events as being loud and of long duration, ultimately requiring a significant amount of exertion, was associated with triggering a migraine. As a result, there were clear avoidance behaviours demonstrated by the participants, particularly around social events and activities that tend to be less mandatory than responsibilities associated with work, for example.

I wouldn't be as up to those social gatherings and even if it was in the middle of the day, say like an afternoon tea now with a load of other women and all that talking... sometimes that buzz or something, I could find maybe an hour or two after that that I start to feel drained and potentially that I could get a migraine in a day or two. (Participant 3)

Weddings would be the kind of the ultimate pinnacle of going on for a long time. So, I'll just avoid going to weddings, you know. Which then, of course, that's when people really get offended because obviously it's such a special thing to them. (Participant 10)

4.3.1.2. Subtheme Two: Self-conscious emotions. (n = 7)

Many participants spoke about feelings of guilt because of not living up to expectations of themselves or expectations by others. Such guilt permeated all social relationships, ranging from professional work relationships to closer friendships. The feelings of guilt associated with cancelling or letting people down acted to push the migraineur not to cancel plans, which *Participant 3* stated “*that's what I try to avoid is that guilt. But that's to my own detriment*” highlighting the consequences of not taking care of themselves when they have a migraine. However, the impact of guilt was clearly expressed as impacting mental well-being too, “*It's awful if you kind of*

feel you're letting other people down. That's always, I think the worst thing."

(Participant 9)

Guilt was largely based on the participants' own beliefs and self-appraisal that they weren't living up to social expectations. This was demonstrated on occasion by participants who even with expressions of understanding from others, found that feelings of guilt persisted, emphasising the role of personal values in experiences of guilt. For example, *participant 8*, spoke of their career as a social worker in which they felt many vulnerable individuals relied on their presence at work and when they had to call in sick due a migraine they were overcome with guilt. These emotions persisted even after reassurance from her superiors:

I'm letting people down; I'm letting the kids down, you know? and I mean, as saying goes like, perspective. The manager was like "Look, we'll sort it out. If we have to cancel that, we'll cancel it. We'll run it again, it's fine". Do you know what I mean? But I just felt I was like, I'm really letting people down, you know. (Participant 8)

This was demonstrated more explicitly by *participant 10* who felt as though the support and understanding received from friends was not adequately reciprocated by themselves due to the time and effort required to try managing and live with migraine, ultimately leaving no time or ability to be present in these friendships.

Luckily, my very good close friends really understand. But I still feel I'm letting them down and it might be quite a while before I see them because I've cancelled once and they're busy and then I feel bad if they have things going on in their life that I'm not supporting, you know, to talk about their stuff as well. (Participant 10)

However, at times, the guilt expressed by participants was based on more clear expressions of disappointment by others “*you inevitably end up sometimes having to disappoint them, and I know they don't always mean to show their disappointment, but you see the disappointment and it's like a double whammy of disappointment*” (Participant 8).

4.3.1.3. Subtheme Three: Acceptance and resilience (n = 7)

The thought of how easily migraine can take over one's life was very prominent among the participants. This worked to create a sense of urgency and necessity around being resilient and not allowing the migraine to control life. In a way, resilience was enabled by not accepting the realities of migraine and pushing on with tasks which would have been seen to trigger or worsen an attack. However, it was also important at times to accept the conditions set out by migraine. As such, there was a careful balancing act of acceptance. Participants reported that it was important to accept the reality of having migraine as being temporarily impaired or disabled to reduce the affective consequence associated with being frustrated and disappointed.

The consequences of being unaccepting of their migraine diagnosis on resilience and the volatile nature of resilience on mental wellbeing were highlighted by some participants who discussed feeling significantly upset at times because of their migraines. The emotional distress for these participants was mediated by unaccepting thoughts around their reality with migraine.

This isn't fair that this is still happening to me, when I am doing everything within my power to prevent it and manage it, and I'm working hard at this. I do sometimes find I can get a little bit like... this isn't fair?

..

Yeah, it's kind of it's upsetting to kind of think... Yeah... I'm not living a life that I should be able to live (Participant 9)

"First of all is it's a bit of, I feel it's a loss, it's a loss of the life I thought I would have" (Participant 10)

Participants expressed separation of themselves and their migraine suggesting a lack of acceptance, viewing the migraine as impacting their life rather than accepting their life with migraine *"I feel like, you know, in the middle of an attack, I'd have often said to my family or, you know, people around me, this is literally ruining my life" (Participant 4)*. There were times when participants recalled moments when they were particularly struggling to cope with their migraine and the related symptoms. In these moments, there were lapses in resilience that enabled help-seeking behaviours. For example, *participant 1* demonstrated months of resilience and coping with dizziness caused by vestibular migraine; however, this left the participant emotionally and physically desperate.

That's what really made me go to the doctor because I said I can't live my life like this. I can't be doing this and like there was a stage where I'd say I was dizzy for about four months, like and I was driving, and I live an hour from my work. So, I'm on a motorway. So, I was driving up and down the road with this dizziness. I was just making sure I wasn't turning my head really quickly or, you know, it was just awful. And I just, I lived in that fuzz for about four months and eventually I went to the doctors. I can't do this. As

soon as I got into the doctor, I start bawling, crying and I said I can't live my life like this. This is desperate. (Participant 1).

Acceptance that, on occasion, migraine would act as a barrier, particularly when an attack has occurred and that the participant would have to endure the attack if necessary. Moments such as these were described by *Participant 1* who stated at times, they had to reframe their thoughts and actively cope by accepting the circumstances of a migraine that is unresponsive to analgesics “*OK, I have the migraine, let's deal with it. There's nothing I can do. Hopefully it'll be gone in an hour or two or tomorrow or whatever day it is*”. However, if the migraine is quite severe and unrelenting, after some time acceptance and resilience may lapse as it becomes harder to cope with the pain and symptoms particularly over an extended period. This was also relative to the participants typical experience of migraine:

I think I have built up resilience. So yeah, when, when my migraines were always three days, on day three, I was unbearable to live with. You know, whereas now I can get... I can manage further. I can keep my resilience going further. I suppose it depends on the level of pain as well. You know the pain, whether the pain level is 6 out of 10 or you know a nine out of 10.
(Participant 10)

4.3.2. Theme Two: *Treatment: Trial and Error* ($n = 10$)

The theme ‘Treatment: Trial and Error’ captured the exploratory nature of the approach to treating migraine. Many participants reported having to trial different medications to find what works for them as one medication that works effectively for one person, isn’t necessarily going to work for the next. As such, this process can be

difficult as participants discuss having to trial medications for months at a time, to ultimately ensure that it is ineffective before moving to another medication. Further, medication effectiveness may also vary situationally and temporally with severe attacks not responding to medication or effectiveness decreasing over time. Participants also expressed a general lack of satisfaction with the professional approach to migraine, often referring to the lack of direction in treatment or, at worst, dismissive attitudes by non-specialist physicians. However, if successful during the trial-and-error process of finding a treatment plan, medication was revolutionary in improving the quality of life and overall ability in the participants. This theme captures the nature of this process as being filled with ups and downs, eliminating medications and physicians to come to a treatment resolution.

4.3.2.1. Subtheme One: Can't rely on medication (n = 9)

Participants mentioned the unreliability of medication due to factors such as not being able to take the medication and medication just not working to prevent or treat the migraine. There were various barriers that participants discussed regarding not being able to take the medication, and these varied from participant to participant; however, they centred around regulations associated with the medications. Of these regulations, pregnancy and breastfeeding were significant barriers for two participants.

Participant 3 was not able to use migraine medication for five years while they started their family between the time when pregnant and then breastfeeding. *Participant 3* mentioned that currently their migraine was much better in comparison to the last “five years of either pregnancy or breastfeeding, I couldn't take any medication like, I actually couldn't go through that again.” Pregnancy and

breastfeeding were also mentioned by *participant 5*, who was discussing their current treatment plan:

So, I'm on that injection with an oral preventative as well. And I was just with my consultant in November and he kind of said that, obviously the injection you've come off at six months before you're thinking of pregnancy and up till November, I thought that that was just going to be me kind of going through that and no help with the tablet form of it. Apparently, you can take it (the tablet) up to a week before you start trying. (Participant 5)

However, other limitations around qualifying for medication included migraine frequency, with one participant mentioning the very clear cut-off for qualifying for a newer injectable medication.

There's this injection, you can get what you have to have, like chronic migraine. So that's more than I think he was saying 15 days a month. So, like if you get 13 days, you know, 13 days of migraine a month, you don't qualify for that. I just think there's very little to help people with migraines. (Participant 4)

Similarly, for *participant 7* who had to stop taking a medication that they found very effective due to how long they had been taking it, due to the health risks associated with long-term usage. As such, they spoke of having to start the process of trialling medications again, further highlighting the impermanent nature of migraine management over time.

However, at times, the participants would decide whether to stop or continue with a medication. For example, *participant 10* was unable to keep taking various medications due to unpleasant side effects. One medication, as *participant 10*

recalled, *“had the side effect of losing weight and I had the side effect of pins and needles and kind of neurological phenomena in my arms and legs”*. The same participant spoke of having to stop another medication in their younger years as it was negatively impacting their ability to perform academically.

One of them was actually in my younger years when I was when I was in university. So, I was probably about 20 and that one made me very, very tired and that was very difficult. So, I had to come off that eventually because I was falling asleep all of the time, in lectures. (Participant 10)

For most participants, however, one of the greatest barriers around not being able to rely on medication was the need to ration the medications, due to the perceived impact too much medication would have on the body in general, and more specifically, the possibility of medication-overuse headache. There was a general understanding that taking too much medication could be detrimental, leading to a situation where participants *“don't want to be jumping to tablets every time”* as it can be quite frequent that participants would need medication *“I get the attacks so often, I can't take the medication that often.” (Participant 10)*.

For a few participants, medication overuse headache was already something they had to contend with, which left them in a worse position than before. Participant 10 stated *“I probably was starting to get into the, the area of medication overuse headache, where I was... the more, more medication I use, the more headaches I was getting, and it wasn't being very effective.”* This was the reality for participant 5 also, who *“had to stop using acute medication in particular paracetamol because I was in the medication overuse migraine”*.

4.3.2.2. Subtheme Two: Lack of Professional Knowledge (n = 8)

Throughout the interviews, many participants expressed a level of discontent with the level of care they received from healthcare providers, often mentioning a lack of professional knowledge on migraine. Access to migraine care varied across participants, with some participants having accessed specialist neurological care via headache clinics and others receiving treatment from their general practitioner. When it came to the care received from general practitioners, participants spoke of a general lack of validation around their migraine and its severity, often receiving suggestions of rather generalised treatment. One participant discussed the difficulty of trying to find a doctor that would take their migraine seriously, *“I could have easily gone through maybe ten plus GPs before I found one that I felt understood what was going on and actually wanted to help”* where the participants prior doctors often dismissed their migraine.

Again, they just didn't understand. Like, here's a prescription for a new contraceptive pill or something like that to manage things. Or maybe, you know, just say, “oh, yeah, just have two paracetamols at a certain time” or “less stress” or “more water” or whatever and nothing ever helped.
(Participant 3)

As mentioned by participant 3, it seemed that general practitioners often approached migraine treatment by trialling medications in a way that seemed experimental; This was also mentioned by Participant 2:

Yeah, I mean, we've tried different things, but to be honest, I was never entirely satisfied like just going through a GP. They just they just tell you,

“these are the latest tablets, try this”. And it always felt a bit of an experiment. (Participant 2)

There were some barriers to accessing specialist care. Participants accessing specialist care through the public health system reported very long waiting lists, while those accessing care privately discussed the significant cost associated with a single appointment. One participant who was entitled to public care spoke of having to pay to be seen privately, as they could not wait the time it would take to be seen:

So, my GP sent an urgent referral, OK to the headache clinic and the waiting list for the urgent referral clinic, the urgent list is 4 years.

I went to see the guy in Dublin and paid €300, and like he was very interested in migraine but he wasn't the least bit interested in me or my, my experience of migraine, I thought, well, that was a total waste of money because everybody's different, you know. (Participant 7)

Like participant 7, many other participants spoke of feeling unsatisfied with specialist care as they were expecting more detailed insight and explanation into their migraine experience, as well as a more innovative and novel approach to care, but were disappointed with the appointment:

I went to a neurologist in the hospital and like, they were quite dismissive as well. He just said like, “oh, you have a migraine brain. You know, your parent if both of your parents have migraines and you're, you're almost guaranteed to have migraines”. (Participant 4)

*There is no private headache clinic in *****, so that's when I went to *****. So, you're supposedly accessing an expert, who doesn't give you the*

time or gives you the time, but it's not, it's not a productive consultation.

(Participant 7)

Treatment at a specialist level was similar to that of general practitioners in that it was still experimental and ultimately involved trialling new medications:

Like I've tried so many different treatments, like and there kind of seems to be, with doctors you kind of have to try Step 1, Step 2, Step 3 see if they work then you move up to step four then you move up to Step 5 and there's been that journey of things working and then things that they're half working and things that are not working . (Participant 8)

One participant had further expressed a lack of knowledge by hospital staff, which was perceived by the participant as being dismissive and condescending:

He gave me a prescription for triptans, and he goes take those and he told me the totally wrong way. But anyway, I always read everything before I take them. And he goes and "that'll, you know, it'll prevent you having to go to your GP and for you to end up here." So basically saying, you know, go away and stop wasting my time. You know, it was terrible. Oh, my God. It was terrible. It was such a bad experience. (Participant 7)

This same healthcare worker refused to send an urgent referral to the headache clinic, ultimately delaying the participant's access to treatment.

He could have because they, the emergency department, have one emergency appointment for that headache clinic. So, if he had taken me seriously, he could have given me that, and that would have been, I would have been three or four months or five months further down the line. (Participant 7)

The nature of treating migraine, being a largely trial-and-error process, meant that many participants spoke of recurring disappointment and feeling frustrated and disheartened by the process.

I just wanted it to work. I wanted results, but they weren't forthcoming.

...

I mean they're just; it's just trial and error and like I don't find it very satisfactory, and they do their best. But like you know it's, it's, I don't know... it's quite a specific treatment. ...And they're just going to try another tablet on you. And I just thought, no, I'm just bored of this because we're just putting in time here. I'm not getting any better. So. (Participant 2)

Well, there you go. I've tried everything and there's nothing else to try. I'm back to managing this myself, so in 2007, I kind of, you know, went back to, I'll, manage this myself.

...

I guess I'm a bit frustrated, going this doesn't work anymore and there's not a huge amount of options available to me anymore. And now that this doesn't work, what am I going to do? (Participant 9)

Due to the lack of support and effective treatment, many participants reported having taken a self-directed approach to treatment, turning to social media and charities such as the Migraine Association of Ireland. Such platforms enabled participants to access knowledge on migraine. Participant 9 spoke about their experience with the Migraine Association Ireland as being the only way of accessing support and useful information on migraine. In discussing the importance of the

association, the participant subconsciously reflects on how little the healthcare system for migraine has changed over the past two decades.

I subscribed and used to get their newsletter, which at the time was just by post. You know, there wasn't much by e-mail back then, and that began to give me a bit of help of realising OK, maybe there's things I can do and then over the years, that's really been the lifeline in getting the information and the help (Participant 9)

The only place that I got any feedback or help is online like, you know, researching myself or going on to Facebook Site or Instagram site? You know with other people that have similar issues or problems? You know, that's the only bit of insight or information that I'd get.

..

Everything you're doing, you're doing what you're deciding yourself to do, you know? (Participant 1).

4.3.2.3. Subtheme Three: Trial and succeed, the benefits of medication (n = 5)

While the trial-and-error process of finding treatment can be particularly difficult, often leaving migraineurs questioning the value of pharmacological approaches and the healthcare professionals who prescribe them, when effective, medication can be extremely important in achieving a sense of normality.

The participants in this study who had found a medication that worked spoke of how it had significantly improved the quality of their life, enabling them to do things that would not have been possible without the medication. For example, Participant 2 spoke of the reassurance of having the medication with them when they

are out, as they can rely on it being effective where in the past a migraine would have dictated their plans:

the whole day isn't gone if you know what I mean?

...

Once I, it's kind of a safety valve and once I know I have it, it's just always it's miraculous. It just works and I have relief and I'm OK again. But in the past, yeah, I've had all that. Where you, you know, you set off somewhere, and I just have to go home or... (Participant 2)

The disparity between life before effective migraine management was made clear by participant five, who stated that before their current medications, they were having daily migraine attacks:

Just one obviously rolled into the next and into the next and then maybe I'd be in the post drome and then another one would come. So, I wouldn't feel like I was ever out of it. A lot of the time at the moment I'm on 2 preventatives and I've had the best, the best kind of quality of life in years. (Participant 5)

Medication, to a large extent, gave the participants back a level of normality that they had been without for so long; they had forgotten what it was like:

*Thankfully, I'm taking ***** and it's working well and what I could not believe when I started taking it, is how quickly it worked and how just how many symptoms went away that I didn't actually even kind of realise were as bad as they were. And I just went to, Oh my God, is this how normal people live? I didn't realise, you know. (Participant 9)*

4.3.3. Theme Three: *Fight for control* (n = 10)

The theme ‘fight for control’ captured the continuous struggle of the participants to control their migraine through prevention and treatment as a means of minimising the impact of migraine on their lives. Part of this need to control was externally motivated by societal pressures of having to ‘keep going’, a reality of living with a sporadic and hidden disability. However, as mentioned in the previous themes, the nature of migraine is that it is unpredictable and means to control through medication can be unreliable. This encapsulates the second subtheme ‘loss of control’ where, despite the participants' active attempts to manage and control the migraine, the migraine persists, and the participants must wait for the migraine to pass and try to cope with the pain. This often impacted the participants' ability to keep up with life. As one participant summarised: *“Yeah, it's hard because the world, the world doesn't stop just because you've a migraine you know and that's really tricky because... you stop, you know? but the world doesn't, and you've commitments and relationships and you know.”* (Participant 8)

4.3.3.1. Subtheme One: *Try to control: I have to keep going* (n = 10)

Throughout the interviews, when talking about what it means to live with migraine, participants expressed the need to keep going, to keep up with day-to-day tasks. This subtheme presents the dichotomy between the active effort made by participants not to let the migraine interfere with life by pushing through an attack, and the inevitable times where migraine does interfere with life, when it came to the pressures of keeping up with life, participants spoke mostly of work, where there was an explicit understanding of the precarious nature of keeping employment as a

migraineur. A migraine attack had the potential to disrupt their ability to work, and in order to maintain employment, there was a need to keep going even during the attack, when in pain. Participants spoke of not only having to make sure they were at work each day but also performing at an appropriate level, highlighting the over-extending approach needed to get by and maintain their livelihood.

“I think it's then when you go into the workplace, these things all become difficult because when you're in the workplace, you've got to perform. You've got to turn up, you've got to.” (Participant 9)

In order to keep up with the demands of life and work, participants described coping strategies of taking large amounts of medication, as a means to keep going.

Even if I was in the post drome phase I would have doped myself up on the painkillers and gone back into work, you know what I mean? because I didn't, you know, the less time I had to take off, the better, you know. And the reality is when I wasn't in work, someone else would have to cover for me and you know, so there was, there was the day-to-day implication even for work, for me not being there, you know. (Participant 8)

For many participants, the effort and push to get through the working week left evenings and weekends as time to recover as much as possible. For some participants, they managed to get through the working week but on those free days is where their migraine would take course.

I suppose it just affected every, every part of my life and I used to manage work, and I'd come home and I'd have to go to bed and wake up, maybe to eat and then go back to bed and then wake up for work the next morning. So, it was kind of a vicious cycle of work, bed, work, bed and a lot of pain.

...

I used to make sure I could get to work, do my work, and then the rest of my life I left to suffer, if you know what I mean. (Participant 5)

Strategies to keep up with life include being prepared for attacks, particularly by having medication on hand to combat the symptoms. For example, participants mentioned they always have acute medication such as analgesics and antiemetics with them, which enabled them to go about their day without as much interference should an attack occur.

I always have antiemetics with me. I'll always have analgesia with me even though I don't take it. I just have it. And... but I and I would take the antiemetic now, I would. (Participant 7)

I would just make sure I have my medication with me and I'm I probably wasn't as good at that in the past, but now I wouldn't go anywhere without it. (Participant 2)

This effort to try to control was evident in day-to-day situations as participants frequently spoke of actively trying to prevent an attack from occurring. How participants tried to prevent attacks varied according to perceived triggers; however, there was a general sense of trying to maintain a balanced lifestyle:

I need to be careful. So, I'll just be a bit more mindful about, like going OK right, have I gotten a bit of fresh air? Have I drunk enough water? Have I had enough sleep? Have I? You know I wouldn't. I wouldn't push it. (Participant 9)

In these ways, whether during an attack or between attacks, participants expressed a need and an active effort to take control of their migraines and the respective impact. This was expressed by overextending during an attack and by taking every precaution to meticulously prevent and be prepared for an attack.

I think in my life for the whole migraine thing, it's kind of trying to keep it under control. The migraine and the pain and the illness or the condition and then trying to control the rest of my life. (Participant 10)

4.3.3.2. Subtheme Two: Loss of Control (n = 10)

This subtheme captures the nature of migraine as a disability that fluctuates over time. Although the participants described an active approach to controlling their migraine, many also acknowledged the impact migraine can have on the ability to function day to day. When asked if they experienced changes in their ability to complete tasks, many of the participants highlighted the disruptive nature of migraine. Participant 7 mentioned “*even simple things like I'll start to do something and then I won't get to finish it*” (Participant 7).

“I could lose two days or three days or, you know, for five days I could be going around like, you know, two days in bed and then three days just not feeling well.” (Participant 9).

The constraints placed on the individual as a result of their condition meant that often it required individuals to utilise the time they spend migraine-free on priority tasks such as work and domestic responsibilities.

And a lot of your interests are the lot of the ideas you might have with the things that you'd like to do. You, kind of never get around to them because

you have to focus your time, that you do have on things that are priorities.

(Participant 5)

However, participants in this study spoke of many areas of their life that are impacted by migraine, including work, socialising, parenting, driving and health (separate to that of migraine). Of these, work, socialising and parenting were mentioned the most frequently. Participants spoke of having to take time off from work, or how they wouldn't be able to perform to their best ability.

The impact on the ability to socialise and attend social events was similar to that experienced at work. Participants recalled disruptions of these events due to having migraines.

Yeah, because it seemed to often be, you know, the slightly, you know, bigger occasions and the excitement of that and... and, you know, all set to go and you're feeling fine. And then it just, you know, just like that then the whole thing changes and you just can't go.

...

Or, or being at something and having to leave early, or, you know, being at a wedding and just having to go to bed for the rest of the day. (Participant 2)

Last year, you know, we had to cancel our holidays. We had to cancel our summer holidays, and we were going to stay with my sisters down the country. Everything was cancelled. I couldn't... I couldn't, you know, go in the car or anything like that, you know. (Participant 7)

Parenting was made particularly difficult by migraine, as participant 3 spoke of their experience being a parent (with migraine) of a newborn baby, to which they

stated, *“you'd have no option to go to bed or anything in that you have to be up and awake with the child”*. Participant 3 spoke of the dependency a young child or baby has on their parent and how having migraine although seriously impaired and in pain, there is no choice to stop. This can be particularly difficult as *participant 3* recalled their experience: *“I would have had the baby on a blanket on the bathroom floor, and my head down the toilet, and I could have been there three hours and trying to breastfeed the child at the same time”* (Participant 3).

The potential of migraine to take full control and disrupt life was emphasised by participant 8 and 10, who had to give up their job as their migraine had become chronic and occurred in at least 15 days each month. The participants had not considered that their migraine would determine their life to such an extent. The following segments highlighted the relationship between the individual and their migraine as a fight for control, which at times, the individual loses. Such cases are particularly difficult as they begin to encroach on identity and wellbeing.

I can wake up any morning, and the migraine is there, and I could have plans for the day and I don't. I just simply don't get them done

...

I all of a sudden find myself, I didn't think when I was... say, let's say 35, that, by the time I was 36, I would be living with chronic migraine and I'd be stuck at home for most of the seven days out of the week, barely able to get up and function. (Participant 8).

I really struggle with that, that I can't work. I don't like using the word 'can't', but that... it's, I'm much better off not working and I struggle with accepting. I do accept it, and I know it's better for me, but I find that quite a

loss and I find how to explain that, how to... what's the word, defend that to other people... I find that very challenging and that affects me mentally I would say. (Participant 10)

4.3.4. Theme Four: *It's not just a headache* ($n = 10$)

The final theme, 'it's not *just* a headache' is comprised of the two subthemes 'The prodrome and postdrome' and 'Social perception of migraine' as it highlights the nature of migraine as being a disorder of the nervous system which involves an array of symptoms separate from headache or pain, contrasting with the social perception of migraine as just a headache.

4.3.4.1. Subtheme One: *The prodrome and postdrome* ($n = 10$)

When participants were asked about whether they felt different in the days preceding an attack, all of them responded yes. In the days leading up to an attack, participants reported autonomic, affective, physiological and cognitive symptoms. Autonomic symptoms were not as commonly endorsed, with only two reporting changes in their perceived body temperature and reported feeling cold in their body.

"I'd be really cold in my body. I don't know for whatever reason, but I'd have it, like a change in body temperature. I'd find I feel really cold. (Participant 8)

"I would feel cold and tired" (Participant 1)

Affective symptoms, such as changes in mood, were more frequent, with participants reporting feeling agitated and irritable, with these mood changes being recognised by those around them.

"I probably wouldn't be in the best mood. I think I'd be more edgy or like, more irritable." (Participant 4)

"I really kind of find myself agitated and cranky with people." (Participant 9)

Other mood changes that were mentioned were feelings of sadness.

Participant 8 stated, "I've noticed I could have a low mood. I could wake up and just be really down in the dumps for, for no reason really. You know what I mean? No identifiable reason." The ability to regulate emotions noted by participant 3 who spoke of getting overwhelmed in the days leading up to an attack and finding it difficult to cope with their usual workload. Participant 3 also mentioned that these feelings of being overwhelmed were usually expressed as frustration and anger, similar to the other participants who reported changes in their mood: "I'm used to having a lot, a lot of open tasks on the go, and then even though I might have the same amount, it all starts feeling very overwhelming, and that I lose kind of control, and then that's when I know the migraine is coming." (Participant 3)

Physical symptoms during the prodrome phase were more frequent, with nine of the ten participants reporting experiencing some sort of change, including body pain, sensations in the head, tiredness and yawning. Feelings of tiredness, a lack of energy or persistent yawning were the most common physical symptoms, reported by eight participants. The feelings of tiredness reported by the participants were suggested to be distinct from typical or expected tiredness and would be quite intense, often accompanied by repeated yawning.

I would be quite tired. No, not every time, but a lot of the time I would be quite tired before a migraine. It's like... it's... it's a different kind of tiredness.

It's not the same tiredness as you'd have like after a day's work. It's literally a tiredness where you just feel like you just need to lie down. You're exhausted and then yawning, I would get a lot of yawning sometimes. (Participant 4)

So, like those can indicate (a migraine coming), if I start yawning, especially out of nowhere, that's a weird one that sometimes that could be a migraine (Participant 5)

Yawning as well and but like a real excessive yawn, like a real pit of your stomach yawn (Participant 8)

Neck pain was reported by four participants and was described as a sensation of stiffness in the neck and shoulders. This was sometimes accompanied by behaviours such as stretching and rolling the neck out to ease the pain and discomfort.

One of them (the symptoms before an attack) is... well it's like I'd get a stiff neck. Especially on one side. So, I'd be kind of like you know, stretching my neck out and trying to get some relief. That usually means I'm getting one (a migraine). (Participant 4)

But a lot of the time now I can go oh, do you know what, I can feel this starting (the migraine). I can feel the tension in my neck... (Participant 9)

This tightness or stiffness in the neck was described by *participant 7* as being mild and at times, difficult to pinpoint as being part of the attack, commenting on the difficulty of isolating the seemingly trivial symptoms in the moment but also recalling them during the interview. Upon reviewing their migraine diary, *participant 7* realised they had documented neck and shoulder pain on multiple

occasions. While not particularly painful, three participants also mentioned feeling sensations in the head in the hours before migraine pain began. This was described as *“heaviness over your head, a kind of a fuzziness in your head. It's not like it's not like a headache. It's just a sensation”* (Participant 2).

Cognitive symptoms that were mentioned as occurring before an attack varied from participant to participant. These were typically reported in relation to the perceived mental ability or how their mental state impacted their ability to perform tasks, with higher-level processing such as problem solving and working memory particularly endorsed.

When I'm getting a migraine, one of my early signs now that I kind of know is actually, if I find I'm being a bit stupid and I can't work things out, that's a bit of a warning to me. Simple stuff that I go, “I should be able to do this. What's wrong with me that I can't do it?” That's always a warning. (Participant 9).

When asked if the participants experienced symptoms in the day(s) following an attack, many agreed and spoke of needing time to recover from the significant toll on the body. Half of the participants spoke of feeling physically and mentally exhausted

“A very low energy absolutely wrecked. I get bad fatigue. Where you feel like you can't even lift your arm.” (Participant 1)

When I come off the migraine, so when the medication kicks in and the pain in the head clears, I'm still very... I don't know, weak? or it takes me a while to come back to where I was before... (Participant 5)

This exhaustion was reported to last two or three days after an attack by participant 10; *“so maybe for two days, if not three days after the pain is gone, I’m very, very tired. You know, exhausted.”* Alongside feelings of fatigue and exhaustion, cognitive symptoms persisted into the days following an attack, with many participants reporting impaired cognitive processes such as decision making. The impaired mental state was sometimes described as “brain fog” (Participant 1, Participant 10). For participant 5, the cognitive impairment was evident through their ability to drive:

“When you normally drive and you can tell that a car is coming and you have an idea of speed and you’ll be, you know, you have time. Whereas I find with migraine, or after a migraine. I don’t have the same judgement”
(Participant 5)

Some participants also touched off having impaired memory following an attack which was quite severe. For example, participant 1 stated *“I could be driving along somewhere and I’m like I don’t. Where am I going again? What am I doing?”* which may suggest impaired working memory. Participant 8 however said when it came to forgetting *“it could be something as simple as my mother saying “Oh, when you can, could you pick this up for me. When you have a chance.” and I totally forget it”* suggesting the potential for impaired prospective memory.

Impaired mood was also reported in the prodrome, with participants reporting feelings of sadness, which seemed to be related to the experience of fatigue.

I don’t have the same energy or the same enthusiasm and the same interest as I would when I’m feeling good. I would say because everything is dulled, I suppose. And I’m tired and I just want to... I need to do nothing. (Participant 5)

4.3.4.2. Subtheme Two: Social Perception (n = 9)

Although the perception of migraine by peers wasn't directly asked about in the interviews, nine of the ten participants discussed the significant lack of understanding by others. The lack of understanding was evident in close relationships with less close acquaintances, where participants stated migraine was seen as *just a headache, just a pain*. The lack of understanding was described clearly by the participants:

I do feel that in general, migraines aren't really recognised properly...

They're just seen as a headache, which is not true. They're very disabling. I'm not able to function when I've got a migraine, a very severe migraine. I can, I can function through a lot of headaches and stuff like that, but when I get a migraine, I can't function at all like... and as well, when I come off the migraine, so when the medication kicks in and the pain in the head clears...

I'm still very I don't know weak, or it takes me a while to come back to where I was before, and I think there's a big lack of understanding in the workplace on that (Participant 6)

I think for a lot of people, the experience is not positive. Because there is this, dismissing or minimising, it's only a headache. No. It's not only headache. And as I was saying, sometimes the headache is the least bad bit, and so do you know that that's I think is a huge thing (Participant 7)

One misconception that was brought up by four of the ten participants was that people often thought they were responsible for their migraine, that “*people think there's a way to avoid it*” (Participant 3). Participant 10 spoke of how this meant that they “*get a lot of, which everyone does, you know, a lot of “helpful” questions.*

Would you not try XY and Z? ”. It became evident throughout the interviews that all relationships, whether acquaintances, work or personal, were affected by migraine. However, in close relationships such as with partners or parents, the lack of understanding was more around less severe attacks, where the symptoms are less visible.

It's, it's easy when you see somebody. On the days where I was couldn't move and in bed, throwing up and whatever, it's easy to see someone and understand them. But the days where you're just feeling only at 50% and going, I just have a bit of a headache. I'm feeling a bit dizzy. I'm feeling a bit sick. I don't want to go into XYZ, I don't want to be in the car for a long time. I don't want to do whatever it is you know. and I that you know, I do think that is that's hard. (Participant 9)

However, at times, the strain on close personal relationships was more explicit as participant 8 spoke of arguments with their husband because of migraine impacting their ability to be present:

*The impact on friends and family and like my partner, my husband as well, it... do you know. We could have plans and that's it then. I'm not sure. I don't feel up to going and yeah, you can. You know, we, we have had arguments. He's been disappointed where he really wants me at something and I couldn't go and you know, you feel really s***, like really because you're letting people down. (Participant 8)*

Moreover, the strain of migraine was particularly detrimental to less salient relationships where there was less understanding and compassion around the participants and their migraine.

So, I have lost a couple of friendships and it's been difficult within my extended family as well. So, some family, not my husband, not my parents, but other family members sometimes have not been very understanding. It's really impacted those relationships.

...

*So have lost friendships and relationships through migraine, without a doubt.
(Participant 10)*

Understanding or lack thereof, acted as a mediator for well-being overall.

While participants spoke of many individuals not being understanding of migraine or not understanding to some degree, they also spoke of situations whereby understanding enabled adaptation of normal life to suit the individual with migraine. The support mentioned by the participants included not having to constantly explain themselves, such as when absent from work, school or social occasions, but also, where possible, adaptations that enabled the migraineur to be present.

I was lucky as well that I had colleagues who were good, and I think probably because they saw me at my worst sometimes. So, they understood it wasn't something I was making up because I had colleagues help me on and off aeroplanes or colleagues in meetings. Kind of, you know, taking over and helping with stuff 'cause they saw I couldn't do something, you know, so it's kind of lucky. (Participant 9)

4.4. Discussion

The results from this study highlighted the reality of migraine as implicating all aspects of the participants' lives and the insufficiency of the approach to migraine treatment in the Republic of Ireland. Numerous issues were highlighted throughout the results of this study, which alongside portraying the lack of access to specialist care, argues for the multidimensional nature of migraine beyond pain and the insufficiency of the current approach to care. Migraine was not limited to pain or even physiological experiences but rather diverged on biopsychosocial facets of lived experience demonstrating the need for a holistic approach to migraine interventions beyond pharmacology (Bolton, 2023; Rosignoli et al., 2022).

Migraine, for many participants, was a source of anxiety due to the unpredictability of the condition. Migraine is unpredictable in that it could occur at any time and any place. Alongside this, the qualities of the attack can differ at each occurrence, such as varying in severity, what symptoms present alongside the migraine, the severity of those symptoms, and the effectiveness of the medication in treating the migraine. The variability of migraine presentation within individuals is clearly documented in the literature (Hansen et al., 2016; Viana et al., 2016). This variability was a source of anxiety-based distress for the participants and was an important factor in the display of avoidance behaviours. Research on migraine has highlighted the high comorbidity of anxiety disorders which have been shown to occur in up to 75% of migraineurs (Breslau, 1998 in Raudenská et al., 2025).

Anxiety in migraine may be that of a psychiatric disorder such as general anxiety or panic disorders or may take the form of anticipatory anxiety and anxiety around causing a migraine (cephalagiaphobia) or the fear of mental exertion as

causing or worsening a migraine (cogniphobia) (Peres et al., 2007; Raudenská et al., 2025). Fear of pain is a concept that has been discussed with regards to various chronic pain conditions such as migraine. In creating a scale to assess fear of migraine, exploratory factor analysis revealed three subscales including fear of negative consequences, attention and anticipation, and fear-avoidance (Klan et al., 2022). Klan et al. (2022) suggest that the factor fear of negative consequences is based on social factors such as having migraine interfere with social commitments and missing out on life. The factor attention and anticipation is guided by the fear of an attack and helps to explain the increased level of self-awareness displayed by individuals with migraine and the general fear of future attacks (Klan et al. 2022). The third factor, fear-avoidance included questions which explored behavioural displays of fear of migraine. The factors outlined by Klan et al. (2022), further align with key points discussed by the participants in this study particularly efforts to control their attacks through careful avoidance of perceived triggers (fear-avoidance), preparation (fear-avoidance) and the impact of not being able to adhere to social obligations (fear of negative consequences). Research has further found that anxiety symptoms were significantly associated with severe migraine-related disability with every 1 standard deviation increase in anxiety symptoms, the odds of severe migraine related disability (MIDAS) were nearly four times as likely (Seng et al., 2017). Findings from Seng et al. (2017) may be explained by the points brought up by participants in this study who spoke about the unpredictable nature of migraine which interfered with their engagement in society such as attending events or changing career with the fear they may not be able to cope or that it might make their migraine worse or migraine would get in the way of their ability to commit to responsibilities.

Participants expressed that they at times mourned the loss of their future and felt aggrieved by their condition, but there was an understanding that this was more harmful and not a sustainable mindset. As such, participants displayed acceptance and resilience towards their migraines and lived reality as a means to keep going, to survive. The display of acceptance and resilience was one that fluctuated with the difficult impact of migraine on the participants where resilience sometimes lapsed when participants experienced significant impairment physically and mentally. The subthemes here at times represent a critical feedback loop whereby anxiety, shame, coping and resilience are integral to the migraineurs experience resembling Troy et al. (2022)' integrative affect regulation framework whereby individuals often fluctuate between positive and negative affective experiences which aid and hinder resilience. This theory of resilience considers different strategies to change the impact of adversity short-term, if positive, enabling long-term resilience (Troy et al., 2022). These strategies were demonstrated by the participants, such as attending their doctor to look for help to *change their situation*, or an understanding that they can't let themselves focus on the negative aspects of migraine, *moving their attention away* from the full extent of the adversity, or *cognitively reconceptualising* their migraine diagnosis by reminding themselves thing could always be worse (Troy et al., 2022). These regulation strategies impact affective experiences and behaviour, social processes, and engagement among others (Troy et al., 2022). However, at times the consequences were more complex and negative including emotions of shame and guilt and working to live up to normative expectations. This was maladaptive for the participants, as it often neglected their individual needs but enabled short-term benefits such as attending work, that prevented long-term resilience as the condition was worsened by over-exertion. As such, the complex

flux of affect regulation, consequences and resilience was a significant narrative of the first theme; Mental wellbeing.

The interactions of the participants with the healthcare system were also a key theme in the data as participants struggled to find medical solutions to their migraine. The participants often felt that the care was inadequate and lacked direction as they were prescribed pharmacological treatments one at a time, trialling the efficacy of each tablet until one worked to prevent or relieve at least some of the migraine attacks. The trial-and-error process in migraine treatment is salient in studies such as Robblee et al. (2020), which found that on average, migraineurs had trialled on average 11 different tablets before trialling the preventative examined in the study. Even the preventative examined in Robblee et al. (2020) found that 28% had stopped taking the medication due its lack of efficacy and side effects. This process was disheartening for the participants and directly impacted their wellbeing as they felt hopeless as each treatment seemed to fail. The development of medication overuse headache is implicated as when treatments are ineffective the consequences of taking excessive medication are not considered (Ruiz de Velasco et al., 2003).

The differences reported by participants on the experience of receiving specialist neurological care or that of a general practitioner was slight. Participants spoke of being dismissed by healthcare workers; a point that has been mentioned by other qualitative studies (Cottrell et al., 2007). Participants were often disappointed in both general practitioners and headache specialists, as they lacked direction in treatment. A study by Young et al. (2019) found that chronic migraineurs frequently reported a lack of satisfaction with care in comparison to episodic migraineurs. In this study, a lack of satisfaction with treatment was particularly difficult for those

who had to wait for a long period to get to the specialist or save up the money to access private care. However, for the participants who were successful in finding a medication that works to treat their migraine, the improvement in their quality of life and ability was significant. The role of medication was evident in the theme ‘fight for control’ where participants actively tried to take control of their migraine through prevention and preparation, where having medication on hand was one of the strategies used to achieve normality. The need to have constant access to medication was further observed by Pirthiraj and Bhagwan (2023), where migraine patients displayed anticipatory anxiety and fear avoidance behaviours. However, even those who had found effective treatment were impacted by migraine as it wasn’t fully reliable and even, and they found themselves at the mercy of an attack, waiting for it to pass. This is in line with research by Lo et al. (2022), who found that acute and preventative treatments for migraine improved health-related quality of life; however, there is a lack of reliability of both treatment types due to varied effectiveness.

The impact of migraine extended beyond the participants and impacted their relationships. Many participants spoke of lost relationships and strain on existing relationships as a result of their migraine and a lack of understanding of the many symptoms that come with the condition, many of which are not visible beyond the afflicted. The impact of migraine on close relationships, such as with partners and spouses, was similar to that reported by Buse et al., (2016), who found that migraine was a source of stress in their relationships. The impact of migraine on the family can be significant, with partners of the migraineur expressing frustration over the circumstances enforced by the migraines, impacting directly on intimacy and the division of labour in the home (Ruiz de Velasco et al., 2003). Results from Buse et

al., (2016), however, also found that migraineurs often overestimated the lack of understanding on behalf of their spouses with regard to the severity of their migraines, suggesting that close relationships may be more understanding than the migraineur believes. The feelings of shame experienced by participants may in part be a result of health-related stigma due to misinformed social understanding of migraine as a headache without fully understanding the scope of the disorder, leading to a discrepancy in the migraineurs' behaviour versus behaviour that is expected. Research on health-related stigma has highlighted that individuals with a disability often internalise the stigma of others regarding their condition. In a study by Young et al., (2013), chronic migraineurs reported high levels of stigma similar to participants with epilepsy; stigma for the migraine group was highly correlated with their inability to work, which was also highest in the chronic migraine group. Another study by Uçan-Tokuç, Göksu and Kati (2024) found that the levels of internalised stigma are even greater for chronic migraineurs with medication overuse headache. Internalised stigma may help to explain the complex feelings of guilt and shame around the impact of migraine on their ability to function in a normative society, views that having migraines is not a disability; it is just a headache and does not justify the behaviour of the individual with the condition (Rutberg & Öhrling, 2012).

With respect to the theoretical frameworks employed in this thesis, the present study touched on the cyclical nature of migraine through the subtheme of *'The prodrome and the postdrome'* in the theme *'It's not just a headache'*. Although it was expected that more detail would be given regarding the questions relevant to capturing phase-related impairment, however participants struggled to recall these symptoms and at times had to be prompted or check their personal migraine diaries.

Those which were recalled, however, were in-line with the hypothesis of hypothalamic dysfunction during the migraine prodrome, such as fatigue, cravings and body temperature changes (Giffin et al., 2003; May & Burstein, 2019; Schult & May, 2016). Such symptoms could be consequential to dysregulated hypothalamic behaviours including sleep, arousal, eating behaviours or hypothalamic neuropeptides such as orexins, and dopamine (Charbit et al., 2010; Holland & Goadsby, 2007). More compellingly, however, the present study highlighted the nature of migraine as a disorder with biological, psychological, behavioural and social manifestations.

There are several points to discuss regarding the transferability and reliability of the findings presented in this study. It may be argued that the sample size of 10 participants and may have impacted the information power or data saturation (Malterud et al., 2016). However, the value of saturation has been critically appraised. Braun and Clarke (2021) argue that determining sample size in qualitative is often pragmatic in nature and emphasise the value of data richness and complexity rather than attaining saturation, in addressing the research question. As such, we argue that the value of the quality of data obtained in the present study was sufficient for its aims. The sample also consisted entirely of participants who were recruited through the Migraine Association of Ireland's various social media outlets. As such, the sample represents a very active and self-directed group of individuals who had reached out for information and support regarding migraine and possibly doesn't represent individuals with migraine who may avoid accessing such services and participating in research due to anxiety, stigma, lack of access and so on. However, the goal of qualitative research is not to produce generalisable findings and the characteristics of the sample and context of the study, should be considered when

determining the transferability to other migraine populations (Drisko, 2024). Similarly, as the primary researcher for this study also has migraine, there was inevitably an impact on the design, interview process, and interpretation of the transcripts. It may be argued that the researcher's personal experience may have enabled bias in selecting themes. However, due to the reoccurrence of certain data points in the interviews and existing literature, and the analytic approach chosen, it is believed that the active and reflexive role of the researcher, particularly one with lived experience, enabled formation of salient themes. As well as this, the researcher's lived experience of migraine helped to develop good rapport with the participants and enabled sharing through a mutual understanding of the migraine experience (Mehrabadi et al., 2024). However, no strategies were used to enhance the credibility of the findings such as the validation of themes by an independent researcher or member-checking, which is a limitation of the present study.

The findings of this study highlight the need for comprehensive, patient-centred care that acknowledges the biopsychosocial impact of migraine as argued by existing research (Rosignoli et al., 2022). There is a need for more psychological interventions for migraine (Sturgeon et al., 2023). The participants in this study expressed the complex impact of migraine on their mental wellbeing through experiences of anxiety, shame and guilt. As such, participants may benefit from cognitive behaviour therapy to reframe their thoughts and beliefs around migraine which could not only lessen the psychological impact of migraine (anxiety, depression, shame) but also migraine outcomes such as migraine frequency (Grazi et al., 2026; Sullivan et al., 2016; Treadwell et al., 2025). Behavioural interventions concerning lifestyle changes are less studied; however, a review by Quartetti et al (2025) found a substantial amount of research indicating a protective role of healthy

diet, regular exercise and good sleep hygiene in migraine. There is a need for peer-support services that aim to increase understanding and coping for individuals with migraine and those around them, as the impact of migraine extends beyond the individual, impacting close relationships most severely. For example, individuals with migraine who feel more socially isolated with reduced support have reported greater migraine impact (Cerami et al., 2021). More research is needed to assess the therapeutic value of peer-support in migraine interventions, although the participants in this study spoke positively of the therapeutic value of peer support through online platforms such as those mediated by the Migraine Association of Ireland. Alongside this, it is evident that large-scale change is needed in the appraisal of migraine at a systemic level, while there is consensus on the suggested standards of care, it is evident through the present study that these are not always met and need to be enabled at a policy level (Steiner et al., 2019; Steiner et al., 2021). The participants in this study expressed difficulty in securing specialist treatment both privately and publicly. A recent study by Vaghi et al. (2023), found that in Ireland, most migraineurs had been diagnosed by general practitioners rather than specialists, emphasising the lack of access to care, which is reserved for more complex migraine cases. General practitioners in Ireland (and Europe) should be provided with advanced education on migraine, given the high frequency of migraine and general primary care being the predominant point of care for the majority of individuals with migraine (Steiner, et al. 2019). Participants availing of public specialists, they reported long waiting periods for their first appointments with headache specialists (Malhan et al., 2022; Raffaelli et al., 2023). Following this, appointments averaged once a year. Participants who accessed private care spoke of the high costs associated with attending specialist care and the monthly cost of medication. As

such, the population of Irish migraineurs could benefit from additional headache clinics, online psychological treatments, and subsidisation of medication costs. Online psychological treatments could not only address the psychosocial dimensions of the condition but enable treatments to reach a greater proportions of the Irish migraine population than the current biomedical approach (Griffiths et al., 2006; Thornicroft & Tansella, 2013) . The findings of the present study support the need for a biopsychosocial understanding of migraine as a complex disorder of the nervous system (Bolton, 2023). Furthermore, increased awareness at policy, healthcare system, and population levels is needed to correct the misrepresentation of migraine as *just a headache* and ultimately enable a holistic approach to migraine care.

Chapter Five

Longitudinal Associations of Behavioural
and Psychological Factors in Migraine
Onset, Characteristics and Phases in Irish
Adult Females.

Abstract

In recent years, migraine research has begun to recognise the condition as a disorder of the nervous system. With this, a new understanding of migraine as being a cycle of phases, of which the migraine headache is preceded by the prodrome phase and followed by the postdrome phase. However, the symptomatic and temporal profile of the pro-and post-drome phases is not yet fully agreed upon in the literature with some studies suggesting high inter- and intra-variability. Furthermore, some phase symptoms such as those related to cognition, are less studied in the research. To do this, a longitudinal design which required participants to complete daily diaries to record migraine attacks (onset, duration, pain severity) alongside homeostatic related symptoms typically reported in the prodrome were used. Participants were further required to wear Fitbit Inspire 2 devices for the study duration. To test frequently reported postdrome cognitive impairment, participants were required to complete remote neuropsychological assessment sessions 24- and 48-hours after three migraine attacks. The data analysis aimed to examine the following: A) the associations of self-reported behaviours and Fitbit variables on the binary dependent variable migraine onset (yes, no). B) the associations of the diary and Fitbit variables from 24-, 48- and 72-hours prior to migraine onset on migraine onset. C) The associations of the diary and Fitbit variables on migraine characteristics as the dependent variables D) The associations between migraine phases and Fitbit and diary variables and E) The associations of session sequence on neuropsychological variables. Findings from the present study indicated a statistical effect of fatigue and fluctuations in eating behaviours and thermoregulation on migraine onset. No significant associations were observed using the lagged predictor variables. Fatigue was also observed to effect migraine duration and severity. A number of associations

with phase were observed alongside statistical differences between phase levels. Findings from the neuropsychological models across assessment sessions observed no detectable pattern in cognitive performance. The findings of the present study warrant further investigation into the role of fatigue, stress, appetite and body temperature in migraine onset. As well as this, greater consideration of suitable neuropsychological measures that withstand repeated measure designs is needed to examine neuropsychological variables across migraine phases.

5.1. Introduction

In recent years, migraine research has suggested that migraine is a dimensional neurological disorder, not simply marked by the characteristic unilateral pain (Karsan & Goadsby, 2021). This has been supported by imaging studies that have found activation of the hypothalamus, basal ganglia, midbrain, pons, spinal trigeminal nuclei and limbic system before the onset of migraine pain (Karsan & Goadsby, 2023). Alongside this, reduced activation has been observed across frontal, temporal, insular, cingulate, and occipital brain regions following a migraine headache, in comparison to interictal functioning (Bose, 2018). Such cortical structures play a central role in regulating physiology, behaviour and cognition; not limited to mood, sleep, appetite changes and autonomic function (Goadsby et al., 2017; Karsan & Goadsby, 2023). While there is a clear overlap in symptoms and cortical structures involved across the phases before and after migraine pain, Bose (2018) highlights the lack of activation in the hypothalamus following an attack, emphasising the distinction between these phases. Collectively, the symptoms occurring before the onset of migraine pain have been denoted as the premonitory phase of migraine or the migraine prodrome, while the symptoms that occur following the cessation of migraine pain are denoted as the migraine postdrome. The clinical manifestation of the migraine phases is not clearly defined. There is a lack of clear temporal and symptomatic boundaries distinguishing the phases (Gollion et al. 2022; Laurell et al., 2016). This is hindered by the nature of the prodrome and postdrome symptoms, which are not indicative of or particular to migraine. That is, migraineurs and non-migraineurs experience most of the associated symptoms regularly (Laurell et al., 2016). Furthermore, the presence of prodromal symptoms does not consistently precede the onset of migraine pain, and not all migraine attacks

are accompanied by a prodrome or postdrome phase (Eigenbrodt et al., 2022; Kelman, 2004). Actually, a substantial number of migraineurs report no change in functioning prior to an attack (Giffin et al., 2003). This may be due to the ordinary nature of the prodromal symptoms and the migraineurs lack of ability to recognise the onset and potential association to the attack (Giffin et al, 2003; Kelman, 2004). It is also suggested that migraineurs may interpret the symptoms of the prodrome as commonly reported migraine ‘triggers’ (Karsan et al., 2021; Schulte et al., 2015).

Despite this, a study by Giffin et al. (2003) using an electronic diary design found that migraineurs experienced an array of symptoms prior to the onset of the migraine headache, including tiredness, stiffness in the neck, increased sensitivity to visual and auditory stimuli and frequent yawning (Giffin et al., 2003). Findings from this study further found that these symptoms were statistically significant in predicting the onset of pain within 72 hours, and similarly, participants themselves were able to predict the onset of pain by acknowledging the onset of these symptoms (Giffin et al., 2003). Postdrome symptoms appear to be similarly frequent, with 81% reporting symptoms such as tiredness, neck stiffness and irritability or more neuropsychological symptoms of light sensitivity and impaired concentration (Giffin et al., 2016). Qualitative studies further emphasise the impact of such non-painful migraine symptoms on quality of life and wellbeing, suggesting that these symptoms at times can be equally as debilitating as the migraine headache (Battista et al., 2023). In line with this, quantitative research has highlighted significant cognitive impairment in individuals with migraine, such as impaired visual and auditory perception, attention, memory and executive functions, compared to healthy, non-migraine controls (Richardson & Diaz-Orueta, 2024). However, several studies have also observed no differences in cognition between individuals with migraine and

non-migraine controls (Richardson & Diaz-Orueta, 2024). This discrepancy in the research may be partially due to case-control study designs, which only assess cognition interictally (between attacks) or during the headache phase, leaving results of little to no cognitive impairment (interictally) or an impairment that is confounded by the experience of pain during the migraine headache (Richardson & Diaz-Orueta, 2024). Such findings further obscure the neurocognitive profile of the disorder within migraineurs and across the literature (Richardson & Diaz-Orueta, 2024).

Further discrepancies in the characterisation of the migraine phases are evident when considering findings by Schwedt et al. (2025), who found that prodrome symptoms were followed by a migraine within a period of only 6 hours in 81.5% of cases, a percentage that decreased to 4.5% of cases after 6 hours. These findings contrast with those of Giffin et al. (2003), who suggest a much longer prodrome window of up to three days. As such, continued longitudinal research into the phases of migraine is needed to clearly characterise the temporal and symptomatic features. The predictive value of migraine prodrome symptoms is of significant therapeutic value by enabling early pharmacological treatment, which is shown to be considerably more effective in treating the symptom of pain and potentially mitigating the migraine headache altogether (Dodick et al., 2023; Lipton et al., 2024; Luciani et al., 2000). Similarly, research into the non-painful symptoms that occur across the migraine phases is needed to develop comprehensive recognition and thereby treatment for migraine as a dimensional neurological disorder. As such to further build on the literature of Schwedt et al (2025) and Giffin et al (2003) and to clarify the symptomatic and temporal profile of migraine, the current study adopts a longitudinal, within and between participant approach to assess behavioural functioning of individuals with migraine across a 90-day period

to examine the influential value of behavioural factors on migraine onset and to characterise behavioural associations within migraine phases. This study will also assess neuropsychological functioning domains of executive functioning and attention in individuals with migraine following a migraine headache compared to functioning between attacks. To do this, Bayesian multi-level models will be used to estimate differences across migraine phases, while accounting for individual variability between participants.

5.2. Methods

5.2.1. Recruitment

Non-random convenience sampling was used to recruit sample of 15 individuals with primary migraine to participate in this study. Recruitment took place from August 2023 until January 2024. Recruitment was conducted alongside the Migraine Association Ireland who distributed the information sheet to the email subscribers, social media platforms, and the charitable association's website (www.migraine.ie). Individuals who were interested in participating were advised to contact the researcher via email. All participants were screened prior to participation regarding the inclusion criteria. The study requirements for inclusion included that the individual be at least 18 years of age, with no existing health condition which may be causing their migraine or a history of psychiatric diagnosis or treatment. These criteria were essential to capture primary migraine in a non-clinical sample and to eliminate potential confounding effects of secondary mental and physical conditions on the behavioural dependent variables. Individuals were also required to be residing in the Republic of Ireland and have daily access to the internet to complete the neuropsychological assessments. Individuals were also briefed on the

requirements of participation which included long-term commitment and a moderate level of technological ability. Following the briefing, if individuals wished to participate, they then were assigned a participant identification number. A consent form containing the information sheet which was also provided by email was posted out to participants and returned via post to the Department of Psychology at Maynooth University alongside the first 30 day completed migraine diary. The sample size and study duration was determined by feasibility and limitations placed on time available and expenses for study materials such as the Fitbit Inspire 2 Devices. This study was approved by the Biological and Biomedical Research Ethics Subcommittee of Maynooth University.

5.2.2. Materials

All participants were provided with information sheets detailing the requirements of the study and participants were briefed on the aims of the study and their rights to participation. All materials required to participate in this study were posted to participants home address. Participants were also provided with return addressed stamped envelopes to post back required materials. All participants received a consent form and instruction sheet to ensure clarity on the study procedure and acquire informed consent. Alongside this, information detailing how to download Fitbit data was also included. Participants were provided with a hard copy, 90-day printed migraine diary. The migraine diary included questions aimed at tracking migraines, common premonitory symptoms, and sleep (see Appendix E). Each participant was also provided with a Fitbit Inspire 2 (FBI2) tracker watch and three stamped and addressed envelopes to return each 30-day cycle of completed migraine diaries and a signed consent form. The Fitbit trackers measured physical

activity (total steps, sleep onset, sleep end, sleep efficiency, resting heartrate, resting heartrate error, root mean square of successive differences in heartrate). Nap duration was also inferred if secondary sleep duration was captured by the FBI2. A validation study by Lim et al. (2023) compared sleep measured by the FBI2 in comparison to polysomnography data in a sample of nine participants. Results from this study found that the FBI2 significantly overestimated total sleep time and rapid eye movement (REM) sleep duration. However, all measures of sleep were overestimated by the FBI2 including total time in bed, sleep efficiency, wake after sleep onset, light sleep (stages 2 and 3), and deep sleep (stage three, slow wave) although these did not reach statistical significance. Findings from Lim et al. (2023) suggested 93.9% sensitivity, 13.1% specificity and 76.0% accuracy in total sleep measurement (see Table 5.1). Low specificity is largely due to the FBI2 recognising lack of movement as sleep behaviour (Lim et al., 2023).

Table 5.1. Table reproduced from Lim et al. (2024), of the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value percentages of the Fitbit Inspire 2 in comparison to polysomnography measurements.

Category	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (5)	NPV (%)
Total Sleep	93.9	13.1	76.0	79.2	38.0
Light Sleep	54.3	62.3	59.1	49.2	67.0
Deep Sleep	84.8	50.1	83.7	98.2	9.5
REM	86.4	59.1	82.3	92.3	43.2

The neuropsychological assessment included the Trail Making Sessions A and B, Cued Go, No/Go test, and Visual Digit Span (Backwards) (Millisecond Software, 2022). In total there were six postdrome neuropsychological assessments and two baseline assessments. To inhibit the effect of practice on the assessment,

each Trail in the Trail Making Test were recoded to include new trails for each assessment. Similarly, for the go no-go test, distinct colour cues were used in each of the assessments and random number sequences in the Visual Digit Span (Backwards) sessions. The alternate stimuli used for the Cued Go, No/Go and the Trail Making Tests can be found in Appendix J. The Trail Making Test utilises two trails, A and B. In Trail A participants are required to connect the dots labelled 1 to 25 in numerical order. In Trail B every second dot has a letter rather than a number, so participants are required to join dots labelled with numbers and then letters in alphanumerical order. For example, 1, A, 2, B, 3, C up to 13, L. The Visual Digit Span (Backwards) displays number sequences that must be recalled in reverse order for 14 separate number sequences. The Cued Go, No-Go Test uses four separate conditions of two cues (horizontal or vertical rectangles) and two targets (colours). The colour of the target is what signals the participant to press or not press the go button. Before the coloured target presents on the screen, the cue (horizontal or vertical rectangles) is presented without any colour. Horizontal cues have a high probability of being go trials while vertical cues have a high probability of being no-go trials. As such, there are no-go vertical and horizontal targets. Online neuropsychological testing was conducted using Millisecond Inquisit Web (Inquisit 6.6.1 [Computer Software], 2022). The assessments were chosen with the intent to examine executive functioning as this cognitive domain has been documented in research to be impacted in individuals with migraine (Richardson & Diaz, 2024). Further consideration was given to the duration of the assessments and the ability to easily modify the tests to create different versions for each assessment session to limit the effect of practice.

5.2.3. Procedure

At the beginning of the study each participant was required to complete a baseline neuropsychological assessment which included the Trail Making Tests A and B, Cued Go / No-Go, and Visual Backwards Digit Span. Participants were required to complete a daily migraine and sleep diary for the full 90-day period of the study. This required participants to answer daily-questions on migraine including if participants had experienced a migraine in the last 24 hours, what time of day it began (morning, afternoon, evening, or night) and how painful the migraine was on a ten-point Likert scale. Participants were asked if they had experienced changes in body temperature (felt unusually cold or unusually warm) or changes in their appetite (have you eaten less than usual, more than usual). Participants were further asked to rate how stressed, fatigued, and unhappy they felt using 10-point Likert scales. Alongside this, participants were asked to record sleep timings including the time they got into bed, the time they tried to sleep, time needed to go asleep, number of wakening's, the time that they woke up at, and the time they got out of bed. Participants were also asked if they woke up earlier or later than they planned and to rate the quality of their sleep using a categorical scale.

Participants were further required to wear the Fitbit Inspire 2 trackers continuously for the full 90-day period of the study except when the device needed to be recharged. It was necessary for participants to synchronise the device daily to the Fitbit mobile app using Bluetooth to ensure all data recorded by the device was stored securely on the Fitbit app and website. Following a migraine, when the pain has ended, participants were required to complete the online neuropsychological assessment twice, 24 hours and 48 hours after the pain has ended. The assessment could be completed on a mobile phone using the Inquisit mobile app or using a

laptop or computer. Time needed to complete the neuropsychological assessments varied; however, it was designed to last approximately 30 minutes. Following each 30-day period participants were required to post the completed 30 days of the migraine diary to the Department of Psychology at Maynooth University and download their Fitbit data (derived from the Fitbit algorithms) for the period. This data was then emailed to the researcher. This was repeated three times throughout the 90-day period (see Figure 5.1). Following completion of the 90 days, a second baseline neuropsychological assessment was issued to participants. Due to unforeseen circumstances, some participants did not complete the entirety of the study; however, any data that was collected during the period was used. In total, 25 individuals agreed to take part in the study; however, the final sample included 15 participants, 13 of whom had completed the full 90-day period. In the same regard, due to missing data related to the Fitbit Inspire 2 devices, and the Fitbit application, some participants completed extra days of the study. Information on each participant's data is available in the Appendices (see Appendix F).

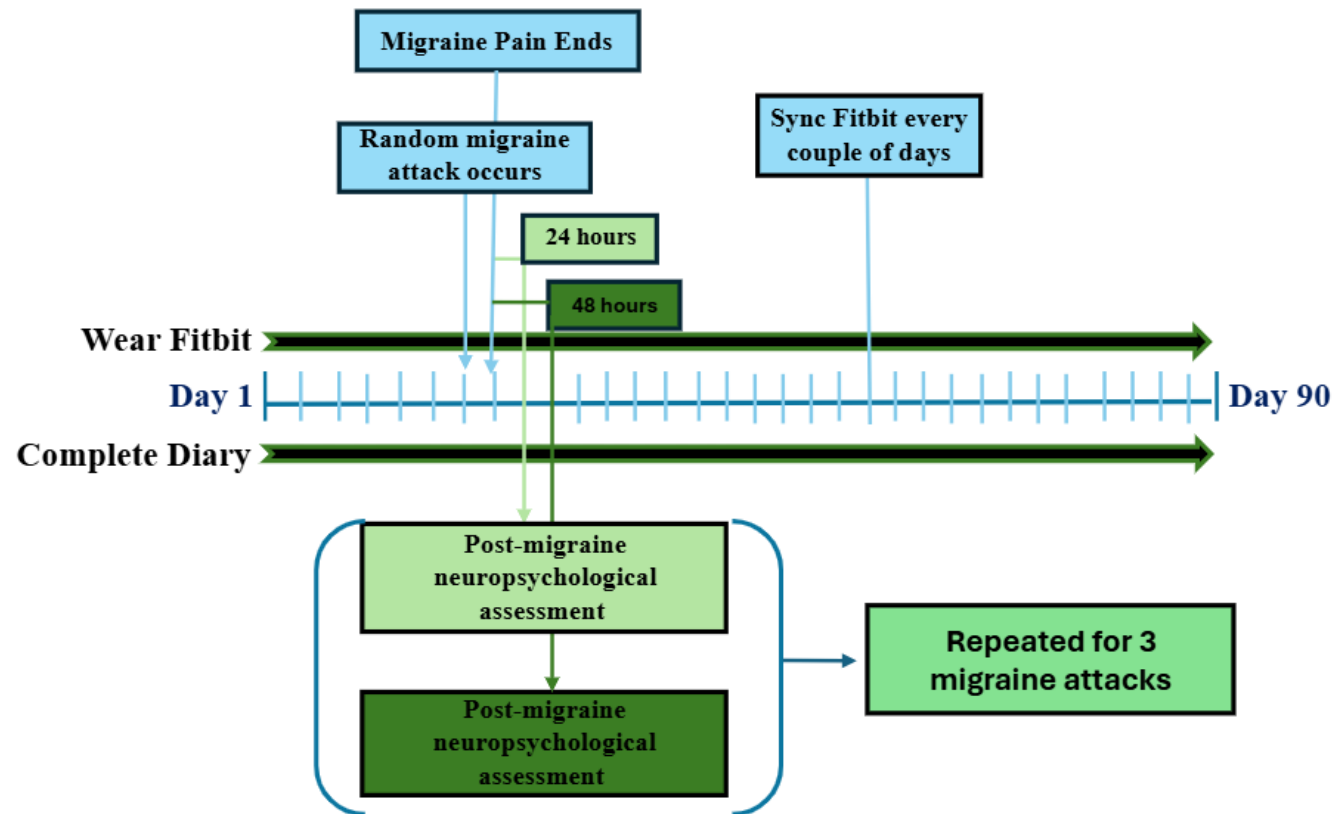


Figure 5.1. Visual depiction of the study procedure over the 90-day period.

5.2.4. Data Input and Variable calculation

All participant data was extracted from the exported Fitbit files sent by the participants. Some data was received in Excel files, or JSON formats that required transformation in Excel. Data that was stored day by day was compiled and data from each variable measured by the Fitbit Inspire 2 active watches were matched to ensure all data was ordered by date. Completed migraine diaries were posted back to the researcher in 30-day intervals. All data from the diaries was manually entered into Excel spreadsheets by the researcher. All Fitbit sleep variables were transformed into decimal values with minutes being a decimal of an hour. For diary sleep variables, sleep onset (time participants tried to sleep + time needed to fall asleep) and sleep duration (sleep onset – sleep end) were calculated. Daily Fitbit step data were compiled to give the total step count for each day. All variables included in the study are detailed below (see Tables 4.2 to 4.4).

5.2.5. Variables

For the neuropsychological assessments, a number of variables were automatically recorded following participation including variables from the practice trials. The output from these trials were not included in the analysis. For the Trail Making Test, the variables that were recorded and included in the analysis were Trail A Error Rate, Trail A Completion Time, Trail B Error Rate, Trail B Completion Time, Total Combined Error Rate and Combined Completion Time. The Visual Digit Span (Backwards) included the variables Backward Two-Error Total Trials (bTETT), Backward Maximum Length (BML), Backward Memory Span (BMS). BTEML is the participants maximum backward digit span. BTETT measures the total number of trials taken until the participant makes two consecutive errors.

BTETT can be interpreted as a measure of consistency. BML measures the maximum digit span that the participant correctly recalls across all trials. BMS represents the digit span that a participant is expected to get correct 50% of the time and is derived from overall performance across all trials and is a more stable measure of memory functioning. The variables included from the Backwards Digit Span were Backward Memory Span (BMS) and Backward Maximum Length (BML). The Go/No-Go test included the variables time taken to complete the test, combined error rate including omission and commission errors, number of errors in the Go trials (omission errors), number of errors in the No-Go trials (commission errors), combined errors for vertical cues, combined errors for horizontal cues, omission error rate with Go cue and Go target, commission error rate with Go cue and No-Go targets, omission error rate with No-Go cue and go target, commission error rate with No-Go cue and No-Go target, mean reaction time in go trials, mean reaction time for Go trials with Go cue and Go target, mean reaction time for Go trials with No-Go cue and Go target. For the purpose of this research, the variables included from the Go/ No-Go test were completion time, combined error rate, omission error rate, and commission error rate. The variables that were included were chosen using a bottom-up approach using the primary neuropsychological variables from the sessions as the study had no a priori hypotheses. However, all other variables that were modelled are presented in the appendices (see Appendix G). One exception was made to output variables from the Go/No-Go in the sixth session as there was an error in the test code which meant this data had to be excluded.

Table 5.2. Table outlining the variables measured using the self-report diary which were included in the analysis.

Variable Name	Description	Measurement Type
Pain Duration	How long migraine pain lasted that day (minutes).	Continuous, (minutes). Capped at 1440.
Time of day	The time-of-day migraine occurred.	Ordinal (morning, afternoon, evening, and night).
Pain Severity	How severe the migraine pain was.	Ordinal Scale (1-10) with 1 being 'Not at all' and 10 being 'extremely'.
Increased Appetite	Has the participant experienced an unusual increase in appetite or increased snacking.	Binary (yes, no).
Decreased Appetite	Has the participant experienced an unusual decrease in appetite or snacking.	Binary (yes, no).
Felt Cold	Has the participant felt unusually cold.	Binary (yes, no).
Felt Warm	Has the participant felt unusually warm	Binary (yes, no).
Fatigue	How fatigued has the participant felt today.	Ordinal Scale (1-10) with 1 being 'Not at all' and 10 being 'extremely'.
Stress	How stressed has the participant felt today.	Ordinal Scale (1-10) with 1 being 'Not at all' and 10 being 'extremely'.
Mood	How unhappy has the participant felt today.	Ordinal Scale (1-10) with 1 being 'Not at all' and 10 being 'extremely'.
Go to Sleep Time	What time did the participant try to go to sleep.	Continuous (clock time).
Time to Sleep	How long did it take for the participant to fall asleep.	Continuous (hh.mm).
Sleep Onset	What time did the participant fall asleep. Calculated using Go to Sleep Time and Time to Sleep.	Continuous (clock time).
Sleep Duration	How long did the participant sleep for. Calculated using Sleep Onset and Wakeup.	Continuous (hh.mm).
Sleep Disturbance Frequency	How many times did the participant wake up.	Discrete.
Sleep Disturbance Duration	In total, how long did sleep disturbances last.	Continuous (hh.mm).
Wakeup	What time did the participant wake up.	Continuous (clock time).
Early or Later	Did the participant wake up earlier or later than planned.	Nominal (Yes, earlier; Yes, later, No).
Sleep Quality	How did the participant rate the quality of their sleep.	Ordinal Scale with 1 being very poor and 5 being very good.

Table 5.3. Table outlining the variables obtained from the Fitbit Inspire 2 devices, which were included in the analysis.

Variable	Description	Measurement Type
Fitbit Sleep Onset	What time did the participant fall asleep.	Continuous (clock time).
Fitbit Sleep End	What time did the participant wake up.	Continuous (clock time).
Fitbit Sleep Latency	How long did the participant take to fall asleep.	Continuous (hh.mm).
Fitbit Sleep Duration	Total time spent asleep.	Continuous (hh.mm).
Fitbit Sleep Disturbance	Total time awake after sleep onset.	Continuous (hh.mm).
Fitbit Inertia	Time spent in bed after sleep end.	Continuous (hh.mm).
Fitbit Time in Bed	Total time spent in bed.	Continuous (hh.mm).
Fitbit Sleep Efficiency	Measure of sleep effectiveness. How much time in bed was spent sleeping.	Ordinal scale (1 to 100).
Mean Resting Heartrate	Number of heart beats per minute during sedentary periods. Divided by the number of daily observations to create the mean resting heartrate.	Continuous.
Entropy	Daily heartbeat irregularity. Higher entropy values suggest greater irregularity and healthy autonomic regulation (Voss et al., 2015)	Continuous.
Resting Heartrate Error	Device measurement error associated with resting heartrate.	Continuous,
Root Mean Square of Successive Differences (RMSSD)	Measure of short-term heart-rate variability. Adaptability of heart rate to changing regulatory systems (Voss et al., 2015).	Continuous.
Steps	Total daily step count.	Discrete.
Nap Duration	Secondary sleep duration that is not part of the participants main nightly sleep duration.	Continuous (hh.mm)

Table 5.4. Table outlining the variables obtained from Milliseconds Trail Making Tests A & B, the Cued Go/ No-Go and Visual Backwards Digit Span which were included in the analysis.

Variable	Description	Measurement Type
Session Number	Each neuropsychological session was given a numerical label based on the order of completion.	Categorical. Session 1 (baseline) Session 2 (24 hours after migraine 1) Session 3 (48 hours after migraine 1) Session 4 (24 hours after migraine 2) Session 5 (48 hours after migraine 2) Session 6 (24 hours after migraine 3) Session 7 (48 hours after migraine 3) Session 8 (second baseline)
Trail A Errors	The number of errors made in Trail A which required participants to connect numbers.	Continuous.
Trail A Time	The time taken to complete Trail A.	Continuous (milliseconds).
Trail B Errors	The number of errors made in Trail B which required participants to connect alternating numbers and letters.	Continuous.
Trail B Time	The time taken to complete Trail B.	Continuous (milliseconds).
Total Trail Errors	The combined number of errors made across Trail A and Trail B.	Continuous.
Total Trail Time	The combined time to complete both Trail A and Trail B.	Continuous (milliseconds).
Backward Maximum Length (BML)	Maximal Backward Digit Span that participants recalled correctly across all 14 trials. Represents the maximum span recalled, although may not be consistent.	Continuous.
Backward Memory Span (BMS)	The backward digit span that participants got correct 50% of the time based on overall performance across all trials. Is more consistent across trials.	Continuous.
Cued Go/No-Go Time	The time needed to complete the Cued Go/No-Go test.	Continuous (milliseconds).
Cued Go/No-Go Error	The combined number of errors made across the entire Cued Go/No-Go test.	Continuous.
Omission Error	The combined number of errors made in Go trials. Participants never pressed the space bar.	Continuous.
Commission Error	The combined number of errors made in No-Go trials. Participants pressed the space bar.	Continuous.

5.2.6. Analysis

As migraine varies between and within individuals, it was necessary to use an analytical approach that would account for between and within participant effects. Alongside this, as there are uneven observations across participants and a large number of variables to consider. For these reasons, it was decided that Bayesian modelling would be the most effective way to analyse the data as it enabled using the regularised horseshoe prior (Piironen & Vehtari, 2017). The horseshoe prior is a type of regularization in the Bayesian statistical paradigm that often performs well for high-dimensional datasets (Piironen & Vehtari, 2017). High dimensional datasets contain a large number of variables (dimensions), often comparable to or exceeding the number of observations. Furthermore, it is harder for statistical models to identify meaningful patterns or relationships in sparse data. The horseshoe shrinkage works by allowing each parameter coefficient (β) to be within a certain range based on individual constraints (i.e. local shrinkage parameters λ_j) and a global level of shrinkage (τ), both of which are determined by the data. Each individual constraint (λ_j) follows a half Cauchy distribution with a parameter of one. Irrelevant coefficient terms are shrunk to zero. Models were fitted using the brms R package (Bürkner, 2017). The default horseshoe settings therein ($df = 1$) were preferred to identical model formulations with a larger global shrinkage parameter ($df = 3$) by widely applicable information criterion (WAIC; Watanabe, 2013). Posterior predictive checks were conducted to compare simulated data generated from the model's posterior parameters with the observed dataset, enabling assessment of model adequacy throughout the analysis. For each posterior draw, replicated datasets were generated and their distributions and summary statistics were compared to those of the observed data to evaluate whether the model could reproduce key features such

as distribution, range, mean and other data characteristics. All missing values were removed from the data for model fitting. To be more conservative, the target acceptance probability was increased from the default value (.8) to .97 in some instances to eradicate divergent transitions (numerical errors). To maintain consistency, all models in each section were fitted in the Bayesian paradigm. All statistical modelling was conducted using RStudio (2026.5.0.218).

For clarity, the study was divided into six sections. Section A aims to understand the relationship between all of the variables in the study and the binary outcome variable migraine onset (yes or no). To achieve this, Bayesian Logistic Regression was used. In this section, 10 models were tested with varying conditions of using the full data set, removing variables with 10% missing data, and adding individual slopes to account for individual differences. In Section B, the binary migraine onset variable was kept as the outcome variable. However, in this section, only lagged data from the predictor variables were used. Predictor variables were lagged at 24-, 48- and 72 hours prior to migraine onset = yes. Section C examined the effect of all diary and Fitbit variables on migraine characteristics. Separate models were used for the each of the characteristic variables' migraine duration, pain severity, and migraine time of day. Section D examined each diary and Fitbit variable individually, with phase as the outcome variable. The phase variable included four levels: between migraine attacks (migraine-free, interictal period), the migraine prodrome (24- and 48 hours before migraine pain onset), the migraine headache₂, and the migraine post drome (24- and 48 hours after migraine pain end). This section enabled comparison of migraine phases for each predictor variable. Section E examined cognitive test scores from the Trail Making Tests A and B, the Visual Backward Digit Span and Go/No-Go test. Each test outcome was modelled

separately with test number as the primary predictor variable. The covariates, age and employment were also accounted for in each model. Each test was numbered in the order they were completed, with tests 1 and 8 being completed during the migraine free period, tests 2, 4, and 6 being completed 24 hours after migraine pain has ended and tests 3, 5, and 7 being completed 48 hours after migraine pain has ended. A statistical effect was determined if the 95% highest posterior density credible intervals (95% CrI) did not contain 0.

Table 5.5. Summary table of the aims and analysis conducted in each section of the results.

Section	Aim	Analysis
Section A	To examine what predictor variables statistically affect migraine occurrence.	Bayesian Logistic Regression of the dependent variable Migraine Onset fitted with the regularised horseshoe prior using two data sets. The first data set included all the data excluding highly correlated variables. The second dataset excluded highly correlated variables and variables with more than 10% missing values. Both datasets were modelled to assess the effects of varying degrees of freedom (3, 4 and 5 df respectively). This was repeated in models which accounted for individual variance by enabling a different slope per participant.
Section B	To examine what predictor variables during the prodrome statistically affect ‘clean’ migraine occurrence.	Bayesian Logistic Regression was used to model the dependent variable Clean Migraine Onset which included only migraine attacks which had no overlap in phases. Predictor variables were lagged at 24-, 48-, and 72- hours.
Section C	To examine what predictor variables affect the dependent migraine characteristic variables.	Separate Bayesian Regression models were used to examine which predictor variables affected the dependent variables Pain Duration, Pain Severity and Time of Occurrence.
Section D	To examine the effect of the variable Phase on each of the Diary and Fitbit variables (excluding migraine characteristics) and to assess for differences between levels of Phase.	Separate Bayesian Regression models were used to examine the effect of the predictor variable Phase which had four levels (prodrome, migraine, postdrome and interictal) on all diary and Fitbit variables while controlling for Age, Employment and Migraine Type.
Section E	To examine the effect of session sequence on each of the neuropsychological test outcome variables.	Separate Bayesian Regression models were used to examine the effect of the predictor variable Session which had eight levels (Session 1 (Baseline), Session 2... Session 8) on the neuropsychological test outcome variables while controlling for Age, Employment and Migraine Type.

5.3. Results

5.3.1. Participants

The study sample included 15 participants. All participants in the sample were female. The mean age was 45 years old. Of the 15 participants, 4 participants were diagnosed as having migraine with aura (26.7%), 6 participants were diagnosed as having migraine without aura (40%), and 5 participants were diagnosed as having both migraine with and without aura (33.3%). In total, 1235 days of data were recorded. Of this, there were 923 non-migraine days and 303 migraine days. The majority of migraines recorded by the participants had a morning-onset (47.2%) while night-onset migraine was the least frequent (3%). The average pain duration per migraine day was 478.84 minutes (7:59 hours). The average pain severity was moderate, with a mean score of 5.04 on a 10-point Likert scale where 1 was not at all, and 10 was extremely painful. Mean time of sleep onset recorded by the diary was 24:18 which was comparable to the 24:09 recorded by the Fitbit Inspire 2 trackers. Mean sleep end recorded by the diary was 08:24 and 08:16 by Fitbit Inspire 2 tracker. Using the 5-point sleep quality scale, mean self-reported sleep quality was 3.32 (66% as a percentage of 5) where mean sleep efficiency as measured by the Fitbit tracker was 87.14%. Mean values for all variables measured are outlined in the tables below (see Table 5.6 - Table 5.8).

Table 5.6. Descriptive statistics of diary variables included in the analysis.

Variable	N	Mean	Std. Error	Minimum	Maximum
Age (years)	15	44.73	0.34	27.00	67.00
Pain Duration (minutes)	268	478.84	23.95	30.00	1440.00
Pain Severity	299	5.04	0.10	1.00	10.00
Fatigue	1228	4.89	0.06	1.00	10.00
Mood	1228	3.06	0.05	1.00	10.00
Stress	1227	3.12	0.05	1.00	9.00
Diary Bedtime (hh:mm)	1187	23:31	0:03	15.67	31.42
Diary Sleep Time (hh:mm)	1189	23:50	0:03	15.73	31.42
Diary Time to Fall Asleep (h:m)	1173	0:28	0:01	0.00	6.00
Diary Sleep Onset (hh:mm)	1178	24:18	0:03	15.80	31.50
Diary Sleep Disturbance Frequency	1179	4.56	0.22	0.00	46.00
Diary Total Sleep Disturbance Duration (h:m)	1176	0:34	0:01	0.00	4.00
Diary Wakeup (hh:mm)	1190	7:55	0:03	2.80	17.50
Diary Getup (hh:mm)	1188	8:24	0:03	4.00	17.50
Diary Sleep Duration (h:m)	1179	7:42	0:03	1.28	15.17
Self-reported Sleep Quality	1227	3.32	0.03	1.00	5.00

Table 5.7. Descriptive statistics of Fitbit variables included in the analysis.

Variable	N	Mean	Std. Error	Minimum	Maximum
Fitbit Sleep Onset (hh:mm)	1178	24:09	0:03	15.73	31.42
Fitbit Sleep End (hh:mm)	1178	8:16	0:03	0.22	23.38
Fitbit Sleep Latency (h:m)	1181	0:00	0:00	0.00	0.78
Fitbit Sleep Duration (h:m)	1178	7:09	0:03	0.80	16.50
Fitbit Sleep Disturbance (h:m)	1178	1:00	0:01	0.00	3.02
Fitbit Sleep Inertia (h:m)	1178	0:04	0:00	0.00	1.22
Fitbit Time in Bed (h:m)	1178	8:05	0:03	1.27	19.43
Fitbit Sleep Efficiency	1178	87.14	0.44	33.00	100.00
Fitbit Step Count	1119	8763	136	156	32019
Fitbit Resting Heartrate	1212	68.57	0.22	53.96	89.48
Fitbit Resting Heartrate Error	1203	7.22	0.10	1.23	55.39
Fitbit Entropy	1149	3.29	0.07	1.31	19.43
Fitbit Root Mean Square of Successive Differences	1147	28.72	0.43	7.44	107.49

Table 5.8. Frequency statistics of the diary variables.

Variable	N	Frequency
Participants with Migraine with Aura	4	26.7%
Participants with Migraine without Aura	6	40%
Participants with and without Migraine Aura	5	33.3%
Non-Migraine Days	932	71.8%
Migraine Days	303	23.3%
Morning Onset Migraine	143	47.2%
Afternoon Onset Migraine	107	35.3%
Evening Onset Migraine	40	13.2%
Night Onset Migraine	9	3%
Increased Appetite		
<i>Yes</i>	194	14.9%
<i>No</i>	1016	78.3%
Decreased Appetite		
<i>Yes</i>	69	5.3%
<i>No</i>	1142	88%
Felt Unusually Cold		
<i>Yes</i>	200	15.4%
<i>No</i>	1012	78%
Felt Unusually Warm		
<i>Yes</i>	69	5.3%
<i>No</i>	1143	88.1%
Woke up earlier or later than planned		
<i>No</i>	693	53.4%
<i>Yes, earlier</i>	327	25.2%
<i>Yes, later</i>	190	14.6%

5.3.2. Preliminary Analysis

A correlational analysis was completed to determine the multicollinearity of the variables. To do this, a threshold of .08 was used for the correlation coefficient to determine which variables needed to be removed. Results indicated large correlations in the variables Fitbit Sleep Duration, Fitbit Time in Bed (.97), Diary Bedtime, Diary Sleep time (.94), Diary Wakeup time, Diary Getup time (.90), Sleep Onset, Sleep Time (.85) and Fitbit Sleep End time, and Diary Getup time (.82). It was decided that Fitbit Time in Bed, Diary Bedtime, Diary Getup time and Diary Sleep time would be removed from the models. Similarly, the variable Fitbit time to sleep was removed as this variable contained only the value 0 across all cases and could not explain any variance in the models. In the preliminary analysis, line plots of the participants data were created to visualise functioning during migraine and migraine free days. See figures 5.2 - 5.6 for examples of these visualisations. Further figures can be found in Appendix H.

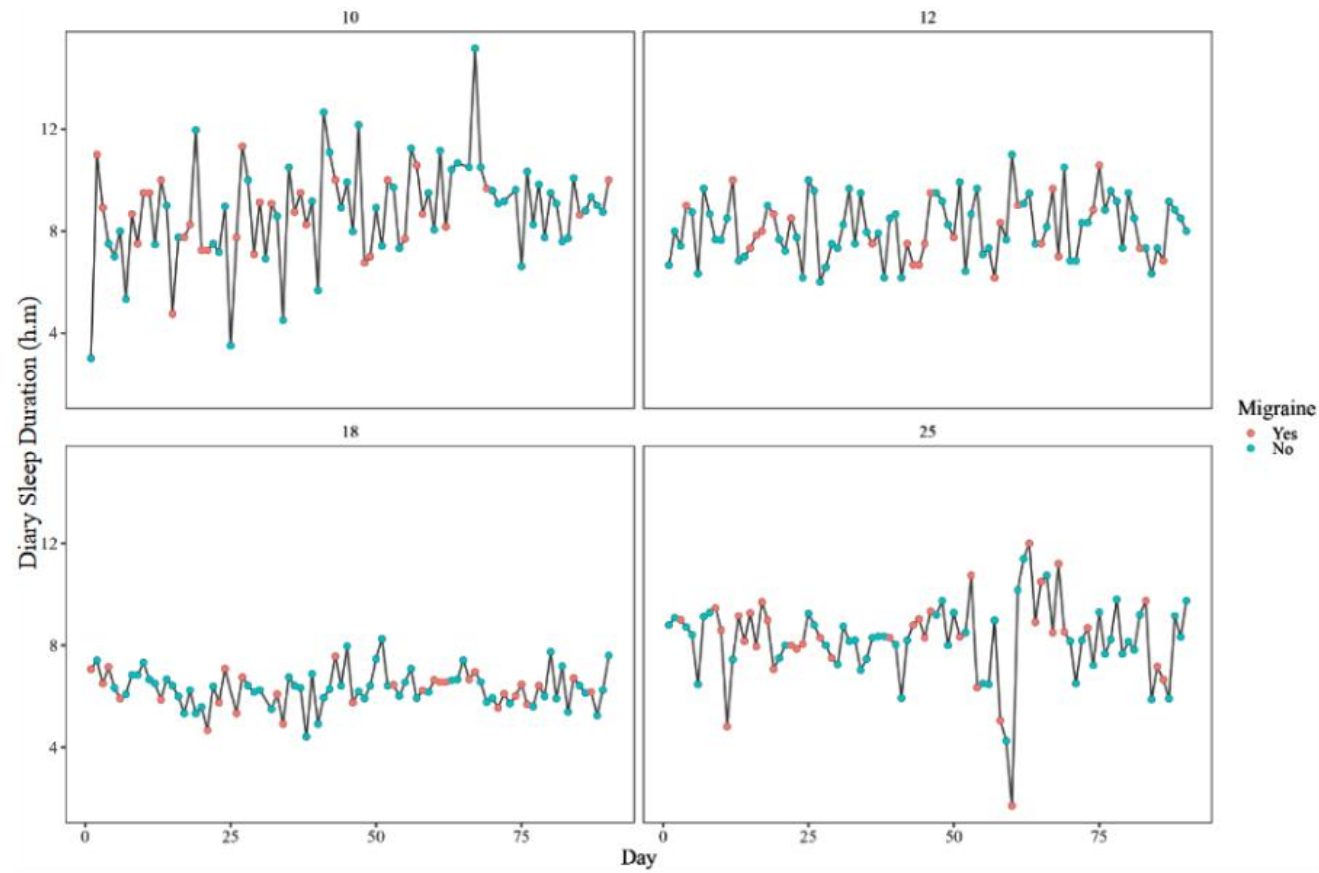


Figure 5.2. Line plots of diary sleep duration (h.m) frequency of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

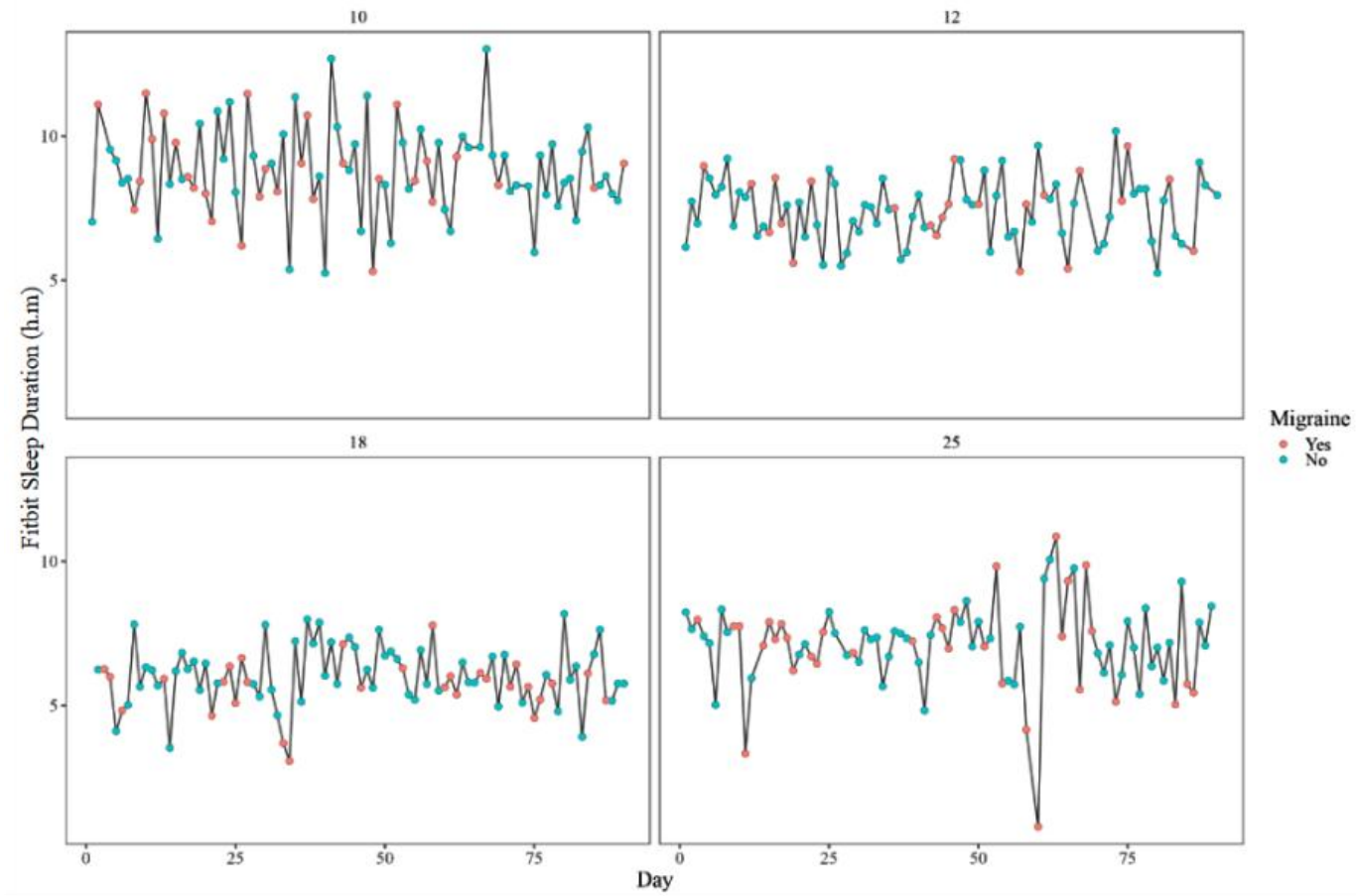


Figure 5.3. Line plots of Fitbit Sleep Duration (h.m) of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

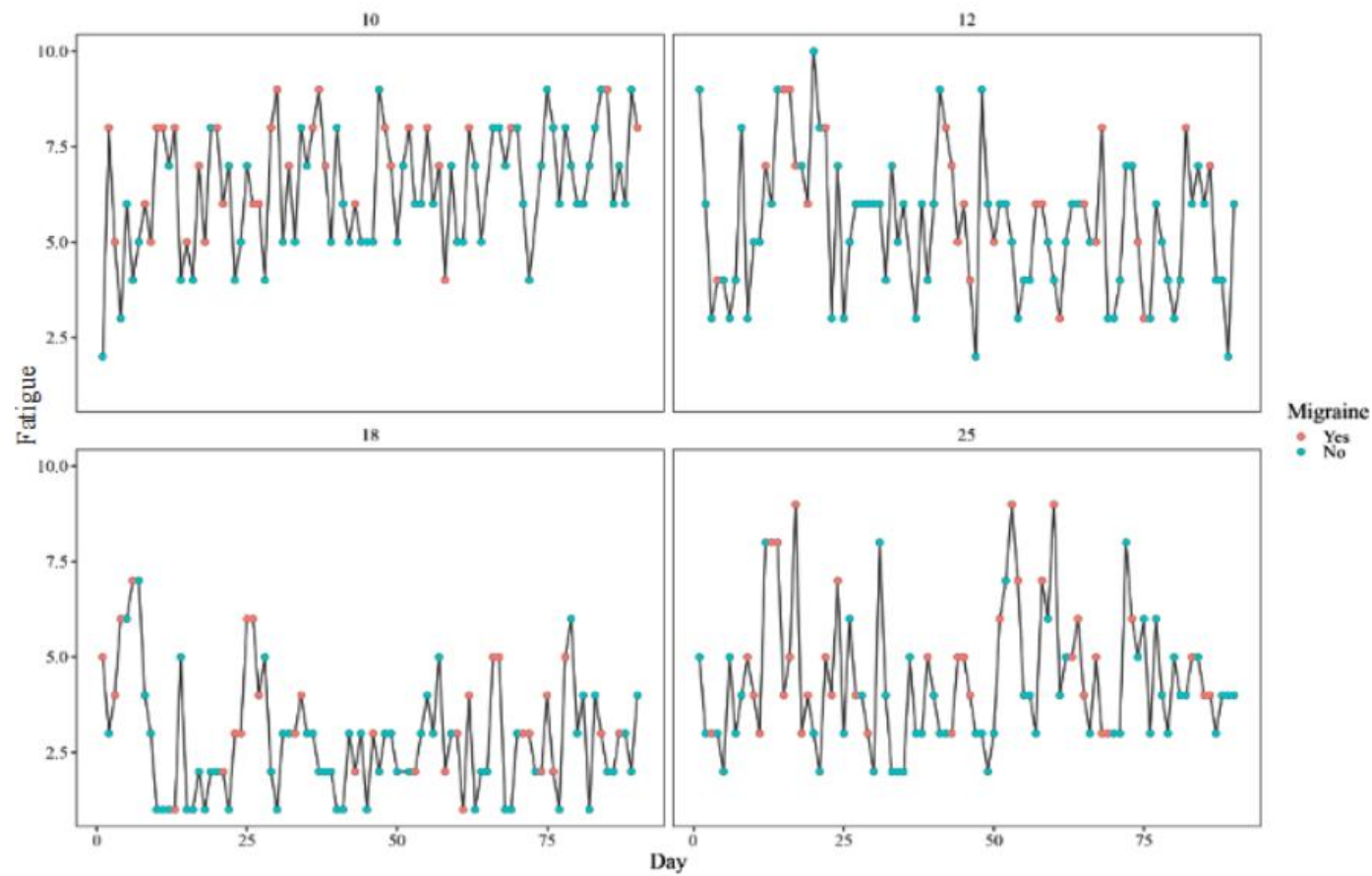


Figure 5.4. Line plots of daily self-reported Fatigue from four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

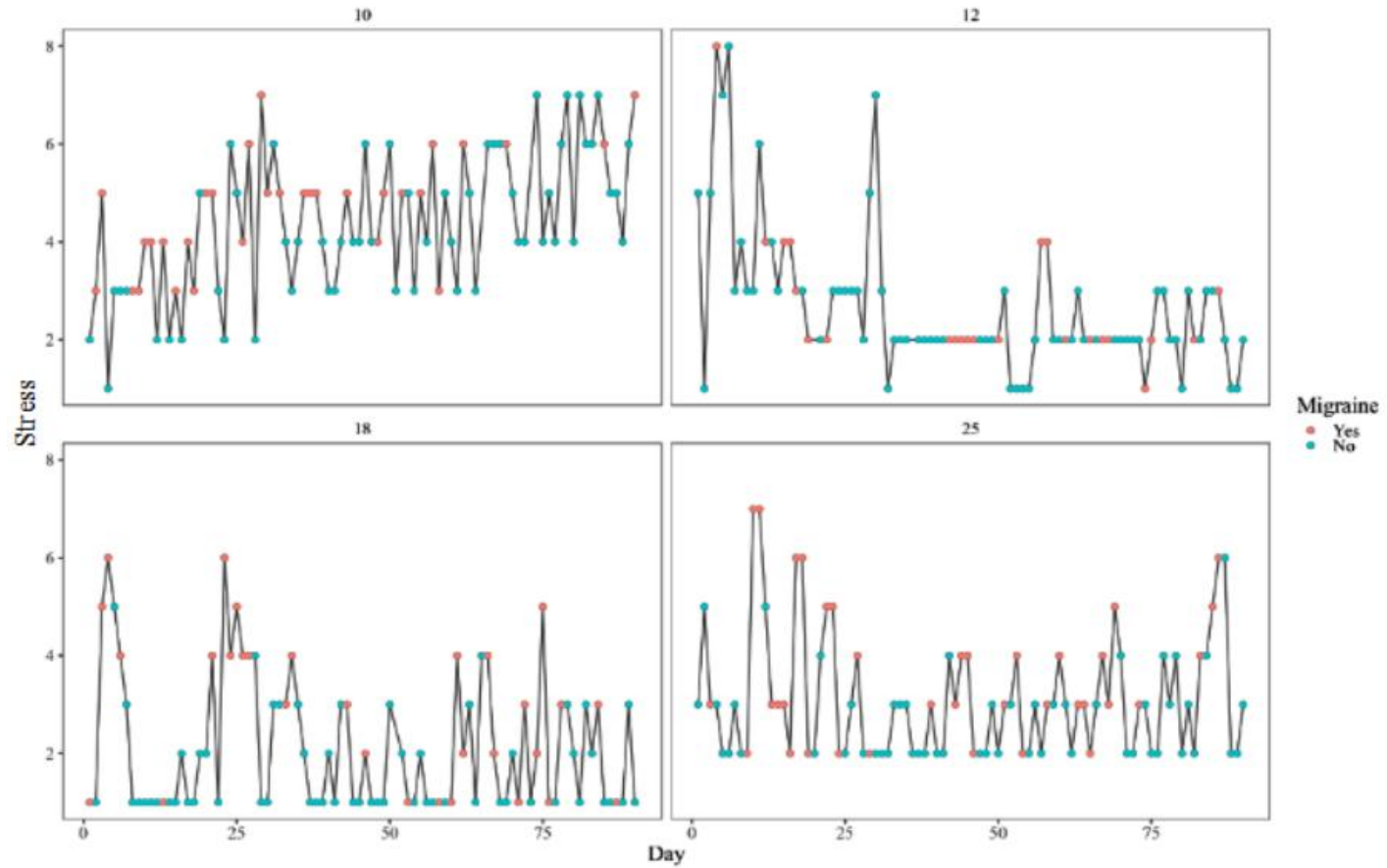


Figure 5.5. Line plots of daily self-reported Stress from four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

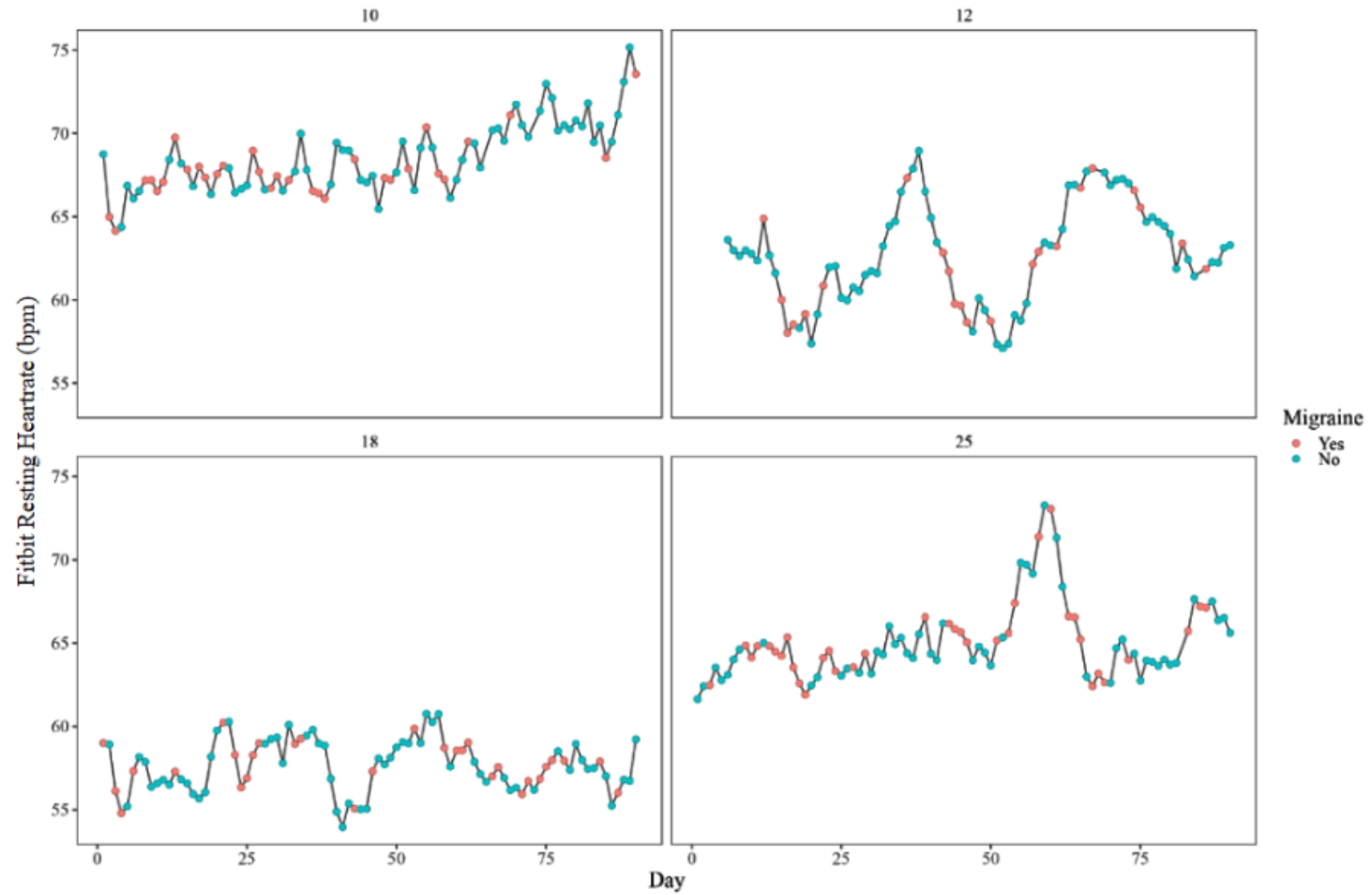


Figure 5.6. Line plots of Fitbit Resting Heartrate of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

5.3.3. Section A: Bayesian Logistic Regression of Migraine Occurrence

In this section, the aim was to investigate which diary and Fitbit variables affected migraine occurrence. It was hoped that this would inform migraine research in detecting important behaviours and affective states which could be investigated as therapeutic targets in future research. In this section, 10 models were assessed to find the best realisation of the data. Models with migraine onset (yes, no) as the response variable were fitted with the Bernoulli distribution and the regularized horseshoe prior (Pironen & Vehtari, 2017). In each of these models, variables which were dependent on migraine occurrence such as migraine characteristics were excluded alongside the variables Fitbit Time in Bed, Diary Bedtime, Diary Getup time and Diary Sleep time which violated the assumption of multicollinearity.

Model 1

The first model was Bayesian Logistic Regression model using the full data set with migraine occurrence as the response variable fitted with the regularised horseshoe prior. The results from model 1 indicated that the variables Felt Cold (95% CrI = [0.04, 1.35]), Fatigue (95% CrI = [0.32, 0.90] and Stress (95% CrI = [0.01, 0.62]) affected migraine occurrence ($R^2 = 0.29$).

Model 2

A second Bayesian Logistic Regression model was fitted that excluded variables with more than 10% missing values to allow for more non-missing observations in the model fit. The variables Entropy, RMSSD, Nap, Nap Duration, and Steps satisfied this condition and were thus excluded from the model. Following this, the model indicated an association of Increased Appetite (95% CrI = [0.12,

1.24)], Decreased Appetite (95% CrI = [0.18, 1.98]), Felt Cold (95% CrI = [0.36, 1.39]) and Fatigue (95% CrI = [0.48, 0.98]) with migraine occurrence ($R^2 = 0.32$).

Models 3, 4 and 5

Models 1 and 2 assumed a linear association between the variables migraine occurrence and day (time). However, visual inspection of the relationship between migraine occurrence and day revealed a non-linear pattern. As such, the third model was fit to the entire data set and used splines to model the temporal variable (day) to capture the non-linear effect. For model 3, the spline was initially specified with three degrees of freedom, allowing the model to bend sufficiently to follow the observed pattern. In model 3, effects of the variables Felt Cold (95% CrI = [0.05, 1.38]), Fatigue (95% CrI = [0.32, 0.90]) and Stress (95% CrI = [0.03, 0.62]) were statistically supported ($R^2 = 0.29$). Again, using the full dataset, Models 4 and 5 increased the flexibility of the variable day to 4 and 5 degrees of freedom, respectively (Wood, 2017). In model 4, with 4 degrees of freedom, the variables Felt Cold (95% CrI = [0.07, 1.37]), Fatigue (95% CrI = [0.31, 0.90]) and Stress (95% CrI = [0.04, 0.62]) affected migraine occurrence ($R^2 = 0.29$). In model 5 with 5 degrees of freedom, the variables Felt Cold (95% CrI = [0.05, 1.36]), Fatigue (95% CrI = [0.32, 0.89]) and Stress (95% CrI = [0.03, 0.64]) affected migraine occurrence ($R^2 = 0.29$).

Models 6, 7, 8

The same splines were then applied to the reduced data set with variables missing 10% of values removed. Model 6 used 3 degrees of freedom and results from this model indicated effects of Increased Appetite (95% CrI = [0.17, 1.25]), Decreased Appetite (95% CrI = [0.23, 1.99]), Felt Cold (95% CrI = [0.37, 1.37]) and

Fatigue (95% CrI = [0.48, 0.99]) ($R^2 = 0.32$). Model 7 with 4 degrees of freedom, yielded a similar result with Increased Appetite (95% CrI = [0.15, 1.24]), Decreased Appetite (95% CrI = [0.18, 2.01]), Felt Cold (95% CrI = [0.35, 1.39]) and Fatigue (95% CrI = [0.47, 1.00]) showing effects on migraine occurrence ($R^2 = 0.32$). Model 8 with 5 degrees of freedom also observed effects of Increased Appetite (95% CrI = [0.11, 1.28]), Decreased Appetite (95% CrI = [0.19, 1.99]), Felt Cold (95% CrI = [0.31, 1.39]) and Fatigue (95% CrI = [0.47, 0.99]) ($R^2 = 0.32$).

Model 9

Model 9 used the full data set and accounted for individual variability in the data by allowing a different slope per participant over time. The results from model 9 were comparable with that of models 1, 3, 4 and 5, with effects observed for Felt Cold (95% CrI = [0.21, 1.47]), Fatigue (95% CrI = [0.33, 0.91]) and Stress (95% CrI = [0.11, 0.70]) ($R^2 = 0.31$).

Model 10

Model 10 used the reduced data set which excluded variables with more than 10% missing values and accounted for individual variability in the data by allowing different slopes per participants (akin to model 9). Results from model 10 found effects of the predictor variables Increased appetite (95% CrI = [0.08, 1.23]), Decreased Appetite, (95% CrI = [0.06, 2.00]) Felt Cold (95% CrI = [0.43, 1.49]), Increased Fatigue (95% CrI = [0.47, 0.98] and Stress (95% CrI = [0.01, 0.55]) ($R^2 = 0.33$).

The favoured models:

Leave-one-out cross validation was used to pick the best-approximating model. Models 1, 3, 4, 5, and 9 used the full data set while models 2, 6, 7, 8 and 10 used the reduced data set. From the models fitted using the full data set, model 9 with individual slopes applied was preferred (see Table 5.9). This model suggests that individuals who felt unusually cold were 2.41 times more likely to have a migraine, with all other variables held constant. For each unit increase in levels of Fatigue, participants were 1.86 times more likely to have a migraine, with all other variables held constant. Similarly, for each unit increase in Stress, the odds of having a migraine increased by 1.51 times, with all other variables held constant.

Table 5.9. Statistically supported associations in Model 9 using the full data set and individual slopes.

Outcome Variable	Predictor	Odds Ratio	Estimate	[95% CrI]
Migraine Onset	Felt Cold	2.41	0.88	[0.21, 1.47]
	Fatigue	1.86	0.62	[0.33, 0.91]
	Stress	1.51	0.41	[0.11, 0.70]

Using the reduced data set, model 10 with the individual slopes applied was preferred (see Table 5.10). In this model the odds of having a migraine increased with the variables Increased Appetite, Decreased Appetite, Felt Cold, and Fatigue, with all other variables held constant. Increased Appetite was associated with a 1.99 times greater risk of migraine onset compared to those who did not have an Increased Appetite. Having a Decreased Appetite had increased the risk of migraine occurrence 2.94 times in comparison to participants with no Decreased Appetite. Participants who felt unusually cold were 2.59 times more likely to have a migraine

than participants who did not feel unusually cold. For each unit increase in Fatigue, the odds of having a migraine increased by 2.08 times. Finally, for each unit increase in stress, the odds of having a migraine increased 1.32 times.

Table 5.10. Statistically supported associations in Model 10 using the reduced data set and individual slopes.

Outcome Variable	Predictor	Odds Ratio	Estimate	[95% CrI]
Migraine Onset	Increased Appetite	1.99	0.69	[0.08, 1.23]
	Decreased Appetite	2.94	1.08	[0.06, 2.00]
	Felt Cold	2.59	0.95	[0.43, 1.49]
	Fatigue	2.08	0.73	[0.48, 0.99]
	Stress	1.32	0.28	[0.01, 0.55]

5.3.4. Section B: Migraine Occurrence with Lagged Predictors

This section aimed to examine which variables in the prodrome phase (24-, 48- and 72 hours prior to migraine onset) of a migraine attack were statistically associated with the upcoming occurrence of a migraine pain onset. To do this, a variable was created indicating migraine attacks which were preceded by four consecutive migraine free days to eliminate days where there were consecutive migraine attacks or an overlap in what may theoretically be a postdrome phase and a prodrome phase simultaneously. The criteria of having four days without a migraine attack enabled 48 hours of postdrome functioning from potential previous attacks and 48 hours of the prodrome for potential following attacks (Giffin et al., 2003). In this model, 24-, 48-, and 72-hour lags were created for all variables excluding migraine characteristics to see if the predictor variables from 24-, 48-, and 72- hours prior to the migraine onset affected migraine occurrence. Age was also lagged as ID 3 turned 49 of day 16 of the study. For this model, variables which included more

than 10% missing values were excluded from the analysis and both unlagged and lagged versions of the predictors were included.

Results from this model found no associations between the regularly spaced migraine onset variable described above and the predictor variables. Fatigue which was shown to effect migraine onset in Section A had no effect on the regularly spaced migraine variable. No statistical effect of unlagged fatigue (95% CrI [0.00 1.08]) or 24- (95% CrI [-0.18, 0.14]), 48- (95% CrI [-0.99, 0.01]) or 72-hour lagged fatigue (95% CrI [-0.43, 0.07]) was observed on the regularly spaced migraine variable. Similarly, no effects of the variables Felt Cold, Increased, or decreased appetite were observed (see Table 5.11).

Table 5.11. Null findings observed for the predictor variable with statistical effects observed in Section B.

Outcome	Lag	Predictor	Estimate	[95% CrI]
Regularly Spaced Migraine Onset	Unlagged	Fatigue	0.63	[0.00, 1.08]
	24-hr lag	Fatigue	-0.01	[-0.18, 0.14]
	48-hr lag	Fatigue	-0.44	[-0.99, 0.01]
	72-hr lag	Fatigue	-0.05	[-0.43, 0.07]
	Unlagged	Felt Cold	0.02	[-0.14, 0.29]
	24-hr lag	Felt Cold	-0.01	[-0.27, 0.18]
	48-hr lag	Felt Cold	-0.05	[-0.67, 0.12]
	Unlagged	Increased Appetite	-0.01	[-0.22, 0.21]
	24-hr lag	Increased Appetite	-0.05	[-0.58, 0.13]
	48-hr lag	Increased Appetite	-0.04	[-0.56, 0.12]
	Unlagged	Decreased Appetite	0.02	[-0.18, 0.41]
	24-hr lag	Decreased Appetite	0.00	[-0.27, 0.27]
	48-hr lag	Decreased Appetite	0.05	[-0.16, 0.67]

5.3.5. Section C: Bayesian Regression of Migraine Characteristics

This section aimed to examine whether any of the variables included in the study affected migraine characteristics including migraine duration, pain severity, and time of pain onset. It was hoped this would answer the research question of whether the diary and Fitbit variables impacted how long a migraine lasted, how severe it was or what time of day it occurred. For these models, the variable migraine onset (yes/no) was excluded as the migraine characteristics are dependent on a yes response to this variable. Similar to the previous sections, the variables Fitbit Time in Bed, Diary Bedtime, Diary Getup time and Diary Sleep time which violated the assumption of multicollinearity were removed. Due to the varying measurement types of each response variable, different model fits were used.

Migraine duration

Bayesian ordinal regression was used to model the ordinal variable migraine duration as the response variable using horseshoe prior shrinkage. The response variable in this section had 3 levels, as guided by previous research by McGinley et al. (2021). The levels included pain that lasted for less than four hours, 4 to less than 12 hours and 12 hours or more. Results from this model indicated an effect of fatigue on migraine duration (95% CrI = [0.21, 1.26]). The cumulative odds ratio was 2.16, indicating that a one-unit increase in fatigue was associated with a 2.16 increase in the odds of being in a higher duration category.

Migraine Severity

Bayesian ordinal regression was used to model the ordinal variable migraine severity as the response variable using the regulated horseshoe prior. Migraine

severity was measured using a 10-point ordinal Likert scale, with 1 indicating no pain and 10 indicating extreme pain. The results from this model indicated an effect of fatigue on migraine severity (95% CrI = [0.73, 1.47]). The cumulative odds ratio was 3.03, indicating that a one-unit increase in fatigue was associated with a 3.03 increase in the odds of experiencing higher pain severity levels.

Time of Migraine Occurrence

Bayesian multinomial regression was fitted with a Cauchy shrinkage prior with time of migraine occurrence as the response variable. This model further excluded the variables Early or Later and Fitbit Sleep Disturbance due to high multicollinearity. Time of migraine occurrence had four levels: morning, afternoon, evening, and night. Results from this model suggested that decreased appetite (95% CrI = [0.06, 3.28], OR= 4.44) and increased stress levels (95% CrI = [0.18, 1.26], OR= 2.03), and increased sleep quality (95% CrI = [0.02, 1.28], OR = 1.86) were associated with increased odds of having a migraine in the afternoon in comparison to the reference level (morning). Increased fatigue levels (95% CrI = [-1.07, -0.06], OR = 0.57) were associated with reduced odds of having a migraine in the afternoon compared to the reference level (morning). No effects of the predictors were observed for evening and nighttime migraine occurrence.

Table 5.12. Summary table of the statistical associations between the outcome and predictor variables observed in Section C.

Outcome Variable	Predictor	Odds Ratio	Estimate	[95% CrI]
Migraine Duration	Fatigue	2.16	.77	[0.21, 1.26]
Pain Severity	Fatigue	3.03	1.11	[0.73, 1.47]
Morning vs. Afternoon Onset	Decreased Appetite	4.44	1.49	[0.06, 3.28]
Morning vs. Afternoon Onset	Stress	2.03	0.71	[0.18, 1.26]
Morning vs. Afternoon Onset	Fatigue	0.57	-0.56	[-1.07, -0.06]
Morning vs. Afternoon Onset	Sleep Quality	1.86	0.62	[0.02, 1.28]

5.3.6. Section D: Bayesian Regression of Migraine Attack Phase

This section aimed to investigate whether there were differences in the diary and Fitbit variables across migraine phases. It was believed that abnormal behaviour would start to be observed in the prodrome and gradually resolve following or during the postdrome phase. Repeated measures analysis of variance was not possible due to the varying number of phase data points per participant. Instead, the categorical variable *phase* with four levels: interictal (between attacks, where migraine onset = no +/- 48 hours), prodrome (24 and 48 hours before migraine onset), migraine days (migraine onset = yes) and postdrome (24 and 48 hours after an attack) was created. For these models, migraine type was recoded to have two levels; migraine without aura (reference) and migraine with aura. Employment had four levels, unemployed (reference), employed part-time, employed full-time and part-time study/ part-time employed. Only phases with no overlap in the time points were included in the

analysis. All models in this section were fitted with an interaction term between the phase variable and the covariates and then simplified if necessary. Pairwise comparisons were also completed on adjusted levels of the dependent variables between phase levels for all models excluding those with ordinal outcome variables, which were not supported.

5.3.6.1. Diary variables

Fatigue

A Bayesian ordinal regression model was used to assess the relationship between levels of the dependent variable fatigue and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no direct effects between fatigue and phase. A phase specific effect of migraine type was observed with migraine with aura displaying greater fatigue in the prodrome phase compared to migraine without aura in the interictal phase (95% CrI = [0.54, 2.19]). Similarly, a phase specific effect of full-time employment compared to part-time employment was observed with decreased fatigue levels in the migraine phase compared to the reference, interictal phase (95% CrI = [-1.90, -0.05]). Pairwise comparisons were not conducted for ordinal models.

Mood

A Bayesian ordinal regression model was used to assess the relationship between levels of the dependent variable mood and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no direct effects between mood and phase. A phase specific effect of age was observed in the postdrome phase compared to interictally, with increasing age causing reduced unhappiness during the postdrome (95% CrI = [-1.31, -0.12]). A

phase specific effect of employment (retired) was also observed with retired participants displaying reduced unhappiness in the migraine phase (95% CrI = [-3.54, -0.05]). Pairwise comparisons were not conducted for ordinal dependent variables.

Stress

A Bayesian ordinal regression model was used to assess the relationship between levels of stress and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effects of phase on the dependent variable stress. Pairwise comparisons were not conducted for ordinal dependent variables.

Bedtime

A Bayesian Gamma regression model was used to assess the relationship between the variable diary bedtime and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated that there were no effects of phase on bedtime. Pairwise comparisons indicated no differences between phases.

Go to Sleep Time

A Bayesian Gamma regression model was used to assess the relationship between the variable diary sleep time and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated that there were no effects of phase on go to sleep time. Pairwise comparisons indicated no differences between phases.

Self-Report Time Needed to Fall Asleep

A Bayesian Gamma regression model was used to assess the relationship between the variable diary time needed to fall asleep and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effect of phase on time needed to fall asleep. An effect of the covariate variable day was found with reduced time needed to sleep with increasing day (95% CrI = [-0.15, -0.02]). Pairwise comparisons indicated no differences between phases.

Sleep Onset Time

A Bayesian Gamma regression model was used to assess the relationship between the variable diary sleep onset and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated that there were no effects of phase on sleep onset. An effect of employment was observed with individuals in full-time employment displaying earlier sleep onset than the reference group, part-time employment (95% CrI = [-0.09, -0.01]). However, pairwise comparisons revealed a slightly earlier sleep onset in the interictal phase (95% HPD CrI = [0.98, 0.99], MR = .99) and prodrome phase compared to the migraine phase (95% HPD CrI = [0.97, 0.99], MR = .98).

Sleep Disturbance Frequency

A Bayesian Poisson regression model was used to assess the relationship between the dependent variable diary sleep disturbance frequency and phase. The model was adjusted for the covariates day, age, migraine type, and employment. Results from the model indicated no effects of phase on sleep disturbance frequency. Pairwise multiple comparisons revealed reduced sleep disturbance frequency in the prodrome phase compared to the migraine phase (95% HPD CrI = [0.799, 0.998],

incidence rate ratio (IRR) = .90). In the prodrome phase sleep disturbance frequency was approximately 10% lower than in the migraine phase.

Total Sleep Disturbance (h)

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable diary total sleep disturbance and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no differences between total sleep disturbance and phase. A small effect of day was observed with reduced sleep disturbance duration with increasing day (95% CrI = [-0.19, -0.01]). Pairwise comparisons indicated no difference in sleep disturbance duration between phases.

Diary Wakeup Time

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable diary wake up time and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effects of phase on diary wakeup time. Pairwise comparisons revealed earlier wakeup times in the prodrome phase compared to the migraine phase (95% HPD CrI = [0.948, 0.998], MR = .97).

Diary Getup Time

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable diary get up time and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effects between get up time and phase. Similarly, pairwise comparisons revealed no differences in diary get up times between phase levels.

Sleep Duration

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable diary sleep duration and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effects between sleep duration and phase. An effect of employment was observed with increased sleep duration in retired participants (95% CrI = [0.11, 0.55]). Pairwise comparisons revealed no difference in sleep duration times between phase levels.

Sleep Quality

A Bayesian ordinal regression model was used to assess the relationship between the dependent variable sleep quality and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effect of the predictor variables on sleep quality. Pairwise comparisons were not conducted for ordinal dependent variables.

5.3.6.2. Fitbit Variables

Fitbit Sleep Onset

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable Fitbit sleep onset and phase. The model included the covariates day, age, migraine type, and employment. Results from the model suggested no effects of phase on sleep onset. An effect of employment was observed, with full-time individuals sleeping less than the part-time employed reference group (95% CrI = [-.10, -0.01]). Pairwise comparisons indicated no differences between phases.

Fitbit Sleep End

A Bayesian Gaussian regression model was used to assess the relationship between the dependent variable Fitbit sleep end and phase. The model included the covariates day, age, migraine type, and employment. Results from the model suggested no effects of phase on Fitbit sleep end. Similarly, pairwise comparisons indicated no differences between phase levels.

Fitbit Sleep Duration

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable Fitbit sleep duration and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effects of phase on Fitbit sleep duration. Pairwise comparisons indicated no differences between phase levels.

Fitbit Sleep Disturbance

A Bayesian Gaussian regression model was used to assess the relationship between the dependent variable Fitbit sleep disturbance and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effects between Fitbit sleep disturbance and phase. Similarly, pairwise comparisons indicated no differences in sleep disturbance duration between phase levels.

Fitbit Sleep Inertia

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable Fitbit sleep inertia and phase. The model included the covariates day, age, migraine type, and employment. Results from the model

indicated greater Fitbit Sleep Inertia in the postdrome phase compared to the interictal phase. (CrI = [0.05, 0.80], MR = 1.52). In the postdrome phase, Fitbit Sleep Inertia was 52% higher. Pairwise comparisons indicated a reduced Fitbit Sleep Inertia in the interictal (95% HPD CrI = [0.429, 0.916], MR = 0.66), prodrome (95% HPD CrI = [0.310, 0.740], MR = 0.50) and migraine phase (95% HPD CrI = [0.352, 0.772], MR = 0.54). compared to the postdrome phase.

Fitbit Time in Bed

A Bayesian Gaussian regression model was used to assess the relationship between the dependent variable Fitbit time in bed and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effect of phase on Fitbit time in bed. Similarly, pairwise comparison revealed no differences in time in bed duration between phase levels.

Fitbit Sleep Efficiency

A Bayesian ordinal regression model was used to assess the relationship between the dependent variable sleep efficiency and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effect of phase on sleep efficiency. Pairwise comparisons were not conducted for ordinal variables.

Fitbit Daily Step Count

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable Fitbit daily step count and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effect of phase on Fitbit daily step count. An effect of

employment was observed with reduced steps in retired participants compared to part-time employed (95% CrI = [-1.47, -0.01]). Pairwise comparison indicated no differences between phases.

Fitbit Heartrate Entropy

A Bayesian gamma regression model was used to assess the relationship between the dependent variable heart rate entropy and phase. The model included the covariates day, age, migraine type, and employment. Results indicated no effect of phase on between Fitbit heart rate entropy. Similarly, pairwise comparison revealed no differences in heartrate entropy between phase levels.

Fitbit Resting Heartrate Error

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable resting heartrate error and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated increased Resting Heartrate Error in the migraine phase compared to the interictal phase. An effect of employment was observed with reduced steps in retired participants compared to part-time employed (95% CrI = [0,17, 0.28]). A negative effect of day was also observed (95% CrI = [-0.11, -0.06]). Pairwise comparisons indicated reduced resting heartrate error in the interictal (95% HPD CrI = [0.75, 0.85], MR= 0.80). and prodrome phase (95% HPD CrI = [0.75, 0.88], MR= 0.81) in comparison to the migraine phase. Finally, greater resting heartrate was observed in the migraine phase compared to postdrome phase (95% HPD CrI = [1,11, 1.31], MR = 1.20).

Resting Heartrate

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable resting heartrate and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated a negative effect of the prodrome phase on heartrate compared to the interictal phase (95% CrI = [-0.05, -0.01]). A phase specific positive effect of age and resting heartrate was observed between the migraine phase and the interictal phase (95% CrI = 0.01, 0.03]) suggesting increasing age was associated with increasing resting heart rate in the migraine phase compared to the reference interictal phase. Phase specific effects of migraine type were observed in the prodrome and migraine phase (95% CrI = [0.01, 0.03], respectively). Participants with migraine with aura had slightly greater resting heartrate in the prodrome and migraine phases compared to participants with migraine without aura, in the interictal phase. Finally, a phase specific effect of full-time employment was observed in the postdrome phase, compared to part-time employment in the interictal phase (95% CrI = [0.01, 0.05]). Pairwise comparisons indicated greater resting heartrate in the interictal phase compared to the prodrome (95% HPD CrI = [1.01, 1.04], MR = 1.02), migraine (95% HPD CrI = [1.00, 1.03], MR= 1.02), and postdrome phases (95% HPD CrI = [1.00, 1.04], MR= 1.02).

Fitbit Nap Duration (h)

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable nap duration and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated increased nap duration in the prodrome and postdrome phases compared to

the interictal phase (95% CrI = [0.22, 1.41] and 95% CrI = [0, -0.01], respectively). A negative effect of day was observed on nap duration (95% CrI = [-0.46, -0.11]). An effect of age was further observed with increasing age having a negative effect on nap duration (95% CrI = [-3.21, -0.31]). Finally, an effect of employment was observed, with participants in full-time employment napping for less time than participants in part-time employment (95% CrI = [-6.39, -0.17]). Pairwise comparisons indicated reduced nap duration in the interictal phase compared to the prodrome (95% HPD CrI = [0.222, 0.757], MR= 0.46), migraine (95% HPD CrI = [1.174, 2.888], MR= 1.92) and postdrome (95% HPD CrI = [0.219, -0.17], MR= 0.42). Increased nap duration was observed in the prodrome compared to the migraine phase (95% HPD CrI = [1.875, 7.860], MR= 4.23). Reduced nap duration was further observed in the migraine phase compared to the postdrome phase (95% HPD CrI = [0.094, 0.381], MR= 0.22).

Fitbit Root Mean Square of Successive Differences (RMSSD) in Heartrate

A Bayesian Gamma regression model was used to assess the relationship between the dependent variable RMSSD and phase. The model included the covariates day, age, migraine type, and employment. Results from the model indicated no effect of phase on RMSSD. A negative effect of day on RMSSD was observed (95% CrI = [-0.08, -0.13]). Pairwise comparisons indicated no difference in RMSSD between phase levels.

Table 5.13. Summary table of statistical associations observed between the dependent outcome variables and phase levels when compared to the reference interictal phase.

Outcome Variable	Contrast	Odds Ratio	Estimate	[95% CrI]
Fitbit Sleep Inertia	Postdrome / Interictal	1.52	0.42	[0.05, 0.80]
Resting Hearttrate	Prodrome / Interictal	0.97	-0.03	[-0.05, -0.01]
Resting Hearttrate Error	Migraine / Interictal	1.25	0.22	[0.17, 0.28]
Nap Duration	Postdrome / Interictal	2.23	0.87	[0.37, -1.38]
Nap Duration	Prodrome / Interictal	2.39	0.80	[0.22, 1.41]

Table 5.14. Summary table of statistical differences in diary measured dependent outcome variables between phase levels. Statistical effects were determined from 95% Highest Posterior Density (HPD) intervals.

Outcome Variable	Contrast	Odds Ratio	[95% HPD CrI]
Sleep Onset	Interictal / Migraine	0.99	[0.98, 0.99]
Sleep Onset	Prodrome / Migraine	0.99	[0.98, 0.99]
Sleep Disturbance Frequency	Prodrome/ Migraine	0.90	[0.80, 0.99]
Wakeup	Interictal / Migraine	0.97	[0.95, 0.99]

Table 5.15. Summary table of statistical differences in Fitbit measured dependent outcome variables between phase levels. Statistical effects were determined from 95% Highest Posterior Density (HPD) intervals.

Outcome Variable	Contrast	Odds Ratio	[95% HPD CrI]
Sleep Inertia	Interictal / Postdrome	0.66	[0.43, 0.92]
Sleep Inertia	Prodrome / Postdrome	0.50	[0.31, 0.74]
Sleep Inertia	Migraine / Postdrome	0.54	[0.35, 0.77]
Resting Heartrate Error	Interictal / Migraine	0.80	[0.75, 0.85]
Resting Heartrate Error	Prodrome / Migraine	0.81	[0.75, 0.88]
Resting Heartrate Error	Migraine / Postdrome	1.20	[1.11, 1.31]
Nap Duration	Interictal / Postdrome	0.46	[0.22, 0.76]
Nap Duration	Interictal / Migraine	1.92	[1.17, 2.88]
Nap Duration	Interictal / Postdrome	0.44	[0.22, 0.65]
Nap Duration	Prodrome / Migraine	4.23	[1.88, 7.86]
Nap Duration	Migraine / Postdrome	0.22	[0.09, 0.38]
Resting Heartrate	Interictal / Prodrome	1.02	[1.01, 1.04]
Resting Heartrate	Interictal / Migraine	1.02	[1.00, 1.03]
Resting Heartrate	Interictal / Postdrome	1.02	[1.00, 1.04]

5.3.7. Section E: Neuropsychological Assessment

The following section used Bayesian modelling to examine performance in neuropsychological sessions across migraine phases. The study included 8 sessions in total, sessions 1 and 8 were completed during migraine-free periods and represent baseline neuropsychological functioning. Sessions 2 to 7 were completed in the migraine post-drome phase. Sessions 2, 4 and 6 were completed 24 hours after migraine pain had ended and sessions 3, 5 and 7 were completed 48 hours after migraine pain had ended. Due to the structure of the data, each neuropsychological outcome variable from the Trail Making Sessions, Visual Backwards Digit Span and Go/ No-Go were modelled separately with session number as the primary predictor.

The variable session number had eight levels with each level representing the sequence of completion for example, the first baseline was Session 1, and Sessions 2 and 3 were 24- and 48 hours after a migraine and so. Session 1 was the reference level used. For each model, age, migraine type, and employment were included as covariates and a random intercept for participant was included. For this section, migraine type had three levels, migraine with aura (reference), migraine without aura and both migraine with and without aura. Employment had four levels, unemployed (reference) part-time employment, full-time employment, and part-time study/ part-time employment. Pairwise comparisons were completed to examine differences between session levels. Table 5.15 shows summary statistics for each variable across all sessions. For summary statistics of each session, see Appendix I.

Table 5.16. Descriptive summary statistics across all sessions of neuropsychological variables modelled in this section.

Variable	N	Minimum	Maximum	Mean	Std. Error
Trail A Error	83	0	18	2.53	0.34
Trail A Time (ms)	83	24572	296499	102086.67	5826.29
Trail B Error	83	0	20	2.59	0.35
Trail B Time (ms)	83	30701	1097696	94764.34	12973.94
Total Trail Error	83	0	25	5.42	0.56
Total Trail Time (ms)	83	80934.	1267065	210211.96	16031.46
BML	85	3	11	7.45	0.16
BMS	85	3	10	6.92	0.16
Go/ No-Go Time (ms)	76	753624	1495079	803319.78	12227.76
Go/ No-Go Errors	76	0	1	0.09	0.03
Omission Errors	76	0	1	0.11	0.03
Commission Errors	76	0	1	0.08	0.03

5.3.7.1. Trail Making Test

A Bayesian Negative Binomial Type II model was used to examine the dependent variable Trail A error rate with session number as the primary predictor

and age, migraine type, and employment as covariates. A random intercept for participant was included. Model adequacy was assessed via posterior predictive checks. Results from this model suggested that participants made less errors in Trail A across subsequent sessions compared to Session 1 (baseline). Effects of test on Trail A errors were observed in Session 2 (24 hours after migraine 1; 95% CrI = [-3.34, -1.42], IRR = 0.10), Session 5 (48 hours after migraine 2; 95% CrI = [-1.49, -0.11], IRR = 0.46), Session 6 (24 hours after migraine 3; 95% CrI = [-1.83, -0.31], IRR = 0.35), Session 7 (48 hours after migraine 3; 95% CrI = [-1.71, -0.22], IRR = 0.40) and Session 8 (second baseline) (95% CrI = [-1.31, -0.03], IRR = 0.52) and the reference Session 1 (baseline). Pairwise comparisons revealed more Trail A errors in Session 1 compared to Session 2 (see Table 5.17). Differences were further observed between Session 2 and sessions 3 through 8. Compared to Session 2, Trail A errors were less in sessions 3 through 8 (see Table 5.17).

Table 5.17. Pairwise comparisons of Trail A errors between sessions. Statistical effects were determined from 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline/ 24 hrs after Migraine 1 (Session 1 / Session 2)	9.971	3.3861	25.246
Baseline/ 24 hrs after Migraine 3 (Session 1 / Session 6)	2.812	1.0706	5.550
24hrs after Migraine 1/ 48hrs after Migraine 1 (Session 2 / Session 3)	0.187	0.0313	0.428
24hrs after Migraine 1/ 24hrs after Migraine 2 (Session 2 / Session 4)	0.183	0.0313	0.428
24hrs after Migraine 1/ 48hrs after Migraine 2 (Session 2 / Session 5)	0.215	0.0446	0.510
24hrs after Migraine 1/ 24hrs after Migraine 3 (Session 2 / Session 6)	0.283	0.0511	0.704
24hrs after Migraine 1/ 48hrs after Migraine 3 (Session 2 / Session 7)	0.244	0.0549	0.645
24hrs after Migraine 1/ Second Baseline (Session 2 / Session 8)	0.195	0.0505	0.450

A Bayesian Gamma regression model was used to examine the dependent variable Trail A time with session as the primary predictor. The variables age, migraine type and employment were included as covariates. A random intercept for participant was also included. Model adequacy was assessed via posterior predictive checks. Results from the model suggested negative effects of Trail A time with Session 2 (24 hours after migraine; 95% CrI = [-1.07, -0.70]), Session 3 (48 hours after migraine 1; 95% CrI = [-0.49, -0.11]), Session 4 (24 hours after migraine 2; 95% CrI = [-0.44, -0.06]) and Session 8 (second baseline; 95% CrI = [-0.41, -0.05]) compared to the reference Session 1. An effect of age on Trail A time in Session 1 was also observed (95% CrI = [0.05, 0.42]). Increasing age was associated with greater Trail A time in Session 1. Pairwise comparisons revealed differences in Trail A time between sessions. Increased Trail A time was observed in Session 1 compared to sessions 2, 3 and 4 (see Table 5.18). Decreased Trail A time was observed in Session 2 compared to sessions 3 through to 8. Reduced Trail A time was observed in Session 4 compared to Session 5. Finally increased Trail A time was observed in Session 5 compared to Session 8 (see Table 5.18).

Table 5.18. Pairwise comparisons of Trail A completion time between sessions.

Statistical effects were determined by 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline/ 24hrs after Migraine 1 (Session 1 / Session 2)	2.425	2.016	2.903
Baseline/ 48hrs after Migraine 1 (Session 1 / Session 3)	1.346	1.114	1.626
Baseline/ 24hrs after Migraine 2 (Session 1/ Session 4)	1.275	1.044	1.531
Baseline/ Second Baseline (Session 1 / Session 8)	1.256	1.044	1.508
24hrs after Migraine 1/ 48hrs after Migraine 1 (Session 2 /Session 3)	0.554	0.457	0.673
24hrs after Migraine 1/ 24hrs after Migraine 2 (Session 2 / Session 4)	0.526	0.430	0.643
24hrs after Migraine 1/ 48hrs after Migraine 2 (Session 2 / Session 5)	0.416	0.329	0.509
24hrs after Migraine 1/ 24hrs after Migraine 3 (Session 2 / Session 6)	0.497	0.394	0.616
24hrs after Migraine 1 / 48hrs after Migraine 3 (Session 2 / Session 7)	0.488	0.386	0.594
24hrs after Migraine 1 / Second Baseline (Session 2 / Session 8)	0.516	0.425	0.631
48hrs after Migraine 1 / 48hrs after Migraine 2 (Session 3 / Session 5)	0.750	0.586	0.906
24hrs after Migraine 2 / 48hrs after Migraine 3 (Session 4 / Session 5)	0.791	0.635	0.969

A Bayesian Negative Binomial Type II regression model was used to examine the dependent variable Trail B errors with session as the primary predictor and age, migraine type, and employment as covariates. A random intercept for participant was included. Model adequacy was assessed via posterior predictive checks. Results from this model suggested a negative effect of session on the dependent variable in Session 2 (95% CrI = [-2.07, -0.52]), Session 4 (95% CrI = [-

2.19, -0.40]) and Session 7 (95% CrI = [-2.07, -0.29]) in comparison to Trail B errors in the reference Session 1 (baseline). An effect of migraine type was also observed with reduced Trail B errors in individuals with both migraine with and without aura compared to individuals with migraine with aura (95% CrI = [-2.45, -0.27]). A positive effect of employment (retired) was observed on Trail B errors in Session 1 (baseline) (95% CrI = [0.28, 2.63]). Pairwise comparisons revealed greater Trail B error in Session 1 compared to sessions 2 and 4. Reduced Trail B errors were observed in Session 2 compared to Session 6 and Session 8. reduced Trail B errors were observed in Session 3 compared to Session 6. Reduced Trail B errors were observed in Session 4 compared to Session 6 and Session 8. Finally, reduced Trail B errors were observed in Session 5 compared to Session 6 (see Table 5.19).

Table 5.19. Pairwise comparisons of Trail B errors between sessions. Statistical effects determined by 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 24hrs after Migraine 1 (Session 1 / Session 2)	3.577	1.318	7.099
24hrs after Migraine 1 / 24hrs after Migraine 3 (Session 2 / Session 6)	0.179	0.066	0.368
24hrs after Migraine 1 / Second Baseline (Session 2 / Session 8)	0.436	0.125	0.863
48hrs after Migraine 1 / 24hrs after Migraine 3 (Session 3 / Session 6)	0.345	0.128	0.677
24hrs after Migraine 2 / 24hrs after Migraine 3 (Session 4 / Session 6)	0.185	0.054	0.386
48hrs after Migraine 2 / 24hrs after Migraine 3 (Session 5 / Session 6)	0.342	0.118	0.706
24hrs after Migraine 3 / 48hrs after Migraine (Session 6 / Session 7)	4.876	1.686	11.25

A Bayesian Gamma regression model was used to examine the dependent variable Trail B time with session as the primary predictor. Age, migraine type, and employment were included as covariates. A random intercept for participant was also included. Model adequacy was assessed via posterior predictive checks. Results from the model indicated a positive effect of Session 6 compared to the reference level Session 1 (baseline; 95% CrI = [0.24, 0.88]). A negative effect of Session 8 compared to Session 1 was also observed (baseline; 95% CrI = [-0.74, -0.19]). An effect of the covariate age was observed with increasing Trail B time with increasing age (baseline; 95% CrI = [0.08, 0.12]). A positive effect of employment was observed (95% CrI = [0.08, 1.22]). A negative effect of having migraine with and without aura was observed with reduced Trail B time compared to the reference group migraine with aura (95% CrI = [-1.23, -0.19]). Pairwise comparisons revealed increased Trail B time in Session 1 compared to Session 8 and reduced Trail B time in Session 1 compared to Session 6 (see Table 5.20). Reduced Trail B time was further observed for Sessions 2, 3, 4, and 5 compared to Trail B time in Session 6. Increased Trail B time was observed in Session 3 and Session 6 compared to Session 8. Further increased Trail B time was observed in Session 6 compared to Session 7 (see Table 5.20).

Table 5.20. Pairwise comparisons of Trail B completion time between sessions.

Statistical effects were determined by 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 24hrs after Migraine 3 (Session 1 / Session 6)	0.576	0.407	0.775
Baseline / Baseline 2 (Session 1 / Session 8)	1.599	1.210	2.092
24hrs after Migraine 1 / 24hrs after Migraine 3 (Session 2 / Session 6)	0.441	0.304	0.590
48hrs after Migraine 1 / 24hrs after Migraine 3 (Session 3 / Session 6)	0.548	0.371	0.746
48hrs after Migraine 1 / Baseline 2 (Session 3 / Session 8)	1.536	1.124	2.061
24hrs after Migraine 2 / 24hrs after Migraine 3 (Session 4 / Session 6)	0.464	0.325	0.631
48hrs after Migraine 2 / 24hrs after Migraine 3 (Session 5 / Session 6)	0.498	0.346	0.681
24hrs after Migraine 3 / 48hrs after Migraine 3 (Session 6 / Session 7)	2.023	1.386	2.773
24hrs after Migraine 3 / Baseline 2 (Session 6 / Session 8)	2.793	1.873	3.783

A Bayesian Negative Binomial model was used to examine Total Trail Error with session as the primary predictor and age, migraine type, and employment as covariates. A random intercept for participant was included. Model adequacy was assessed via posterior predictive checks. Results from this analysis suggested that in Session 2 (95% CrI = [-2.15, -1.00]), Session 3 (95% CrI = [-1.19, -0.11]), Session 4 (95% CrI = [-1.45, -0.35]), Session 5 (95% CrI = [-1.24, -0.16]), Session 7 (95% CrI = [-1.58, -0.37]) and Session 8 (95% CrI = [-1.06, -0.05]) participants made statistically less errors than in Session 1. A statistical effect for the covariate migraine type was observed with migraine with and without aura; (95% CrI = [-2.04, -0.26]) having reduced Total Trail errors compared to the reference, migraine with

aura. A positive effect of employment was observed (95% CrI = [0.03, 2.00]).

Pairwise comparisons revealed more total Trail errors made in Session 1 compared to sessions 2, 4 and 7. Reduced total Trail errors in Session 2 compared to sessions 3, 4, 5, 6, and 8. Reduced total Trail errors in Session 4 and 5 compared to Session 6 and increased Trail errors in Session 6 compared to Session 7 (see Table 5.21).

Table 5.21. Pairwise comparisons of Total Trail Errors between sessions. Statistical effects were determined by 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 24hrs after Migraine 1 (Session 1 / Session 2)	4.758	2.275	7.900
Baseline / 24hrs after Migraine 2 (Session 1 / Session 4)	2.479	1.314	4.043
Baseline / 48hrs after Migraine 2 (Session 1 / Session 5)	2.018	1.051	3.259
Baseline / 48hrs after Migraine 3 (Session 1 / Session 7)	2.631	1.279	4.544
24hrs after Migraine 1 / 48hrs after Migraine 1 (Session 2 / Session 3)	0.407	0.174	0.702
24hrs after Migraine 1 / 24hrs after Migraine 2 (Session 2 / Session 4)	0.526	0.235	0.935
24hrs after Migraine 1 / 48 hrs after Migraine 2 (Session 2 / Session 5)	0.427	0.190	0.766
24hrs after Migraine 1 / 24hrs after Migraine 3 (Session 2 / Session 6)	0.244	0.109	0.421
24hrs after Migraine 1 / Baseline 2 (Session 2 / Session 8)	0.374	0.161	0.651
24hrs after Migraine 2 / 24hrs after Migraine 3 (Session 4 / Session 6)	0.463	0.235	0.835
48hrs after Migraine 2 / 24hrs after Migraine 3 (Session 5 / Session 6)	0.570	0.280	0.978
24hrs after Migraine 3 / 48hrs after Migraine 3 (Session 6 / Session 7)	2.295	1.009	4.160

A Bayesian Gamma regression model was used to examine the dependent variable Total Trail Time with session as the primary predictor. Age, migraine type, and employment were included as covariates. A random intercept for participant was also included. Model adequacy was assessed via posterior predictive checks. Results from the model suggested a negative effect of Session 2 (95% CrI = [-0.73, -0.34]), Session 4 (95% CrI = [-0.45, -0.03]) and Session 8 (95% CrI = [-0.52, -0.14]) in comparison to total Trail time in the reference Session 1. An effect of migraine type was observed with individuals with migraine with and without aura being associated with reduced total Trail time (95% CrI = [-0.94, -0.01]) compared to individuals with aura. An effect of age was observed with increasing age being associated with increasing total Trail time (95% CrI = [0.09, 0.42]). Pairwise comparisons indicated increased total Trail time in Session 1 compared to Session 2, 4 and 8. Total Trail time was reduced in Session 2 compared to sessions 3 through 7. Similarly, reduced total Trail time was observed in sessions 3, 4 and 5 compared to Session 6 (see Table 5.22).

Table 5.22. Pairwise comparisons of Total Trail completion time between sessions.

Statistical effects were determined by 95% Highest Posterior Density (HPD)

intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 24hrs after Migraine 1 (Session 1 / Session 2)	1.708	1.385	2.045
Baseline / 24hrs after Migraine 2 (Session 1 / Session 4)	1.275	1.017	1.541
Baseline / Baseline 2 (Session 1 / Session 8)	1.395	1.142	1.684
24hrs after Migraine 1 / 48hrs after Migraine 1 (Session 2 / Session 3)	0.712	0.570	0.865
24hrs after Migraine 1 / 24hrs after Migraine 2 (Session 2 / Session 4)	0.745	0.605	0.913
24hrs after Migraine 1 / 48hrs after Migraine 2 (Session 2 / Session 5)	0.637	0.498	0.776
24hrs after Migraine 1 / 24hrs after Migraine 3 (Session 2 / Session 6)	0.476	0.378	0.599
24hrs after Migraine 1 / 48hrs after Migraine 3 (Session 2 / Session 7)	0.700	0.551	0.868
48 hrs after Migraine 1 / 24hrs after Migraine 3 (Session 3 / Session 6)	0.670	0.527	0.846
24hrs after Migraine 2 / 24hrs after Migraine 3 (Session 4 / Session 6)	0.638	0.503	0.796
48hrs after Migraine 2 / 24hrs after Migraine 3 (Session 5 / Session 6)	0.750	0.580	0.924
48hrs after Migraine 2 / Baseline 2 (Session 5 / Session 8)	1.284	1.001	1.572
24hrs after Migraine 3 / 48hrs after Migraine 3 (Session 6 / Session 7)	1.466	1.136	1.826
24hrs after Migraine 3 / Baseline 2 (Session 6 / Session 8)	1.711	1.363	2.175

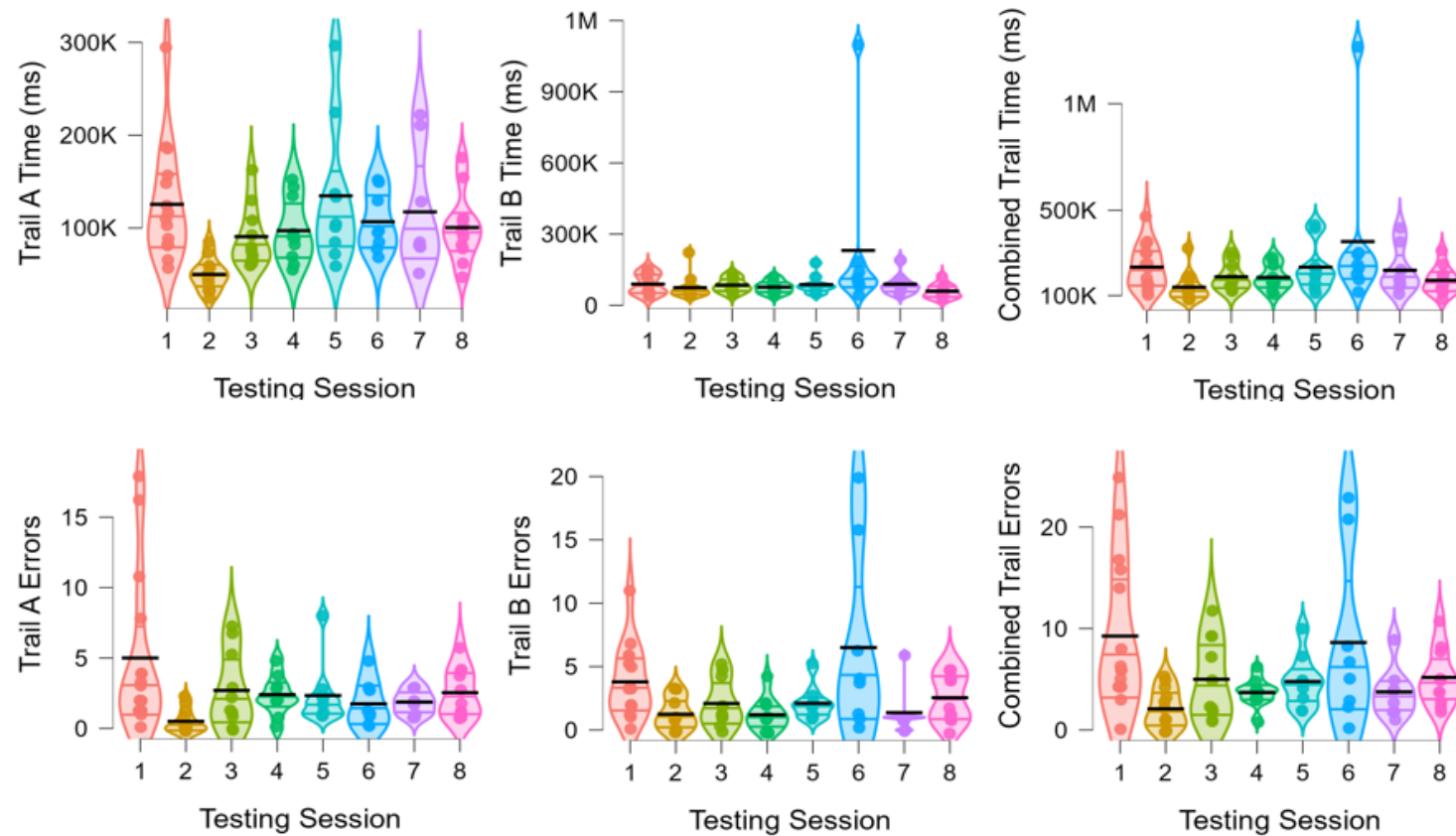


Figure 5.7. Violin plots displaying the distribution of the Trail Making Test variables across sessions. Scatterplots of individual scores are included in each violin with the black line indicating mean values.

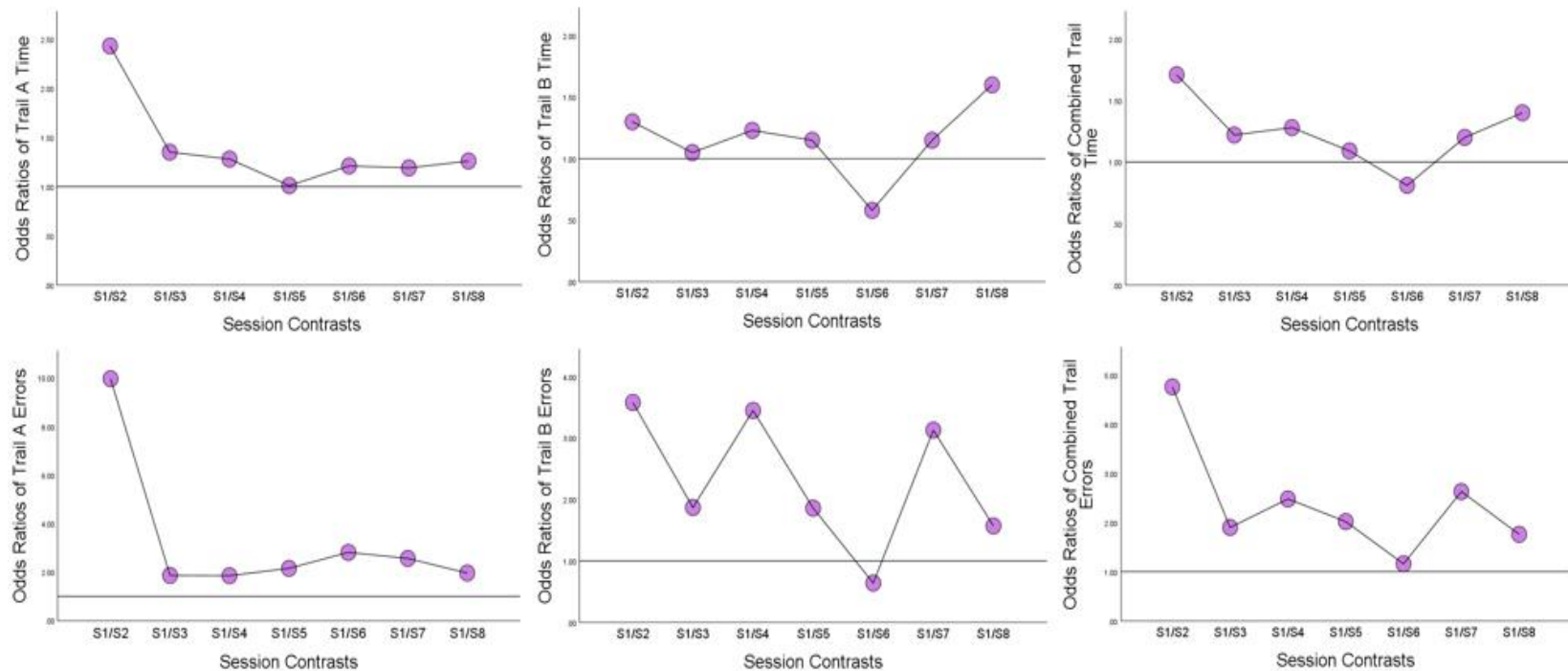


Figure 5.8. Plots of Odds Ratios from session contrasts with baseline (S1). Odds ratios equivalent to 1 indicates scores comparable with baseline (S1). OR contrasts suggest instability of the Trail Making Test variables over time with a trend towards decreased errors and decreased time in all sessions compared to baseline ($OR > 1$). Contrasts between baseline and session 8 (S1/S8) further highlight instability of the test irrespective of migraine effects.

5.3.7.2. Visual Backwards Digit Span

A Bayesian Gamma regression model was used to examine the dependent variable Backward Memory Span (BMS) using session as the primary predictor and age, migraine type, and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from this model indicated a positive effect of sessions 5 (48 hours after migraine 2; 95% CrI = [0.10, 0.37]) and Session 7 (48 hours after migraine 3; 95% CrI = [0.03, 0.31]) compared to BMS scores during the reference Session 1 (baseline). Pairwise comparisons revealed reduced BMS scores in Session 1 compared to sessions 5 and 7. Reduced BMS scores were observed in sessions 2 and 4 compared to Session 5. Finally, increased BMS scores were observed in Session 5 compared to sessions 6 and 8 (see Table 5.23).

Table 5.23. Pairwise comparisons of Backward Memory Span (BMS) between sessions. Statistical effects were determined by 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 48hrs after Migraine 2 (Session 1 / Session 5)	0.787	0.686	0.901
Baseline / 48hrs after Migraine 3 (Session 1 / Session 7)	0.841	0.730	0.961
24 hrs after Migraine 1 / 48hrs after Migraine 2 (Session 2 / Session 5)	0.848	0.736	0.969
24hrs after Migraine 2 / 48hrs after Migraine 2 (Session 4 / Session 5)	0.858	0.747	0.989
48hrs after Migraine 2 / 24hrs after Migraine 3 (Session 5 / Session 6)	1.176	1.010	1.352
48hrs after Migraine 2 / Baseline 2 (Session 5 / Session 8)	1.230	1.062	1.414

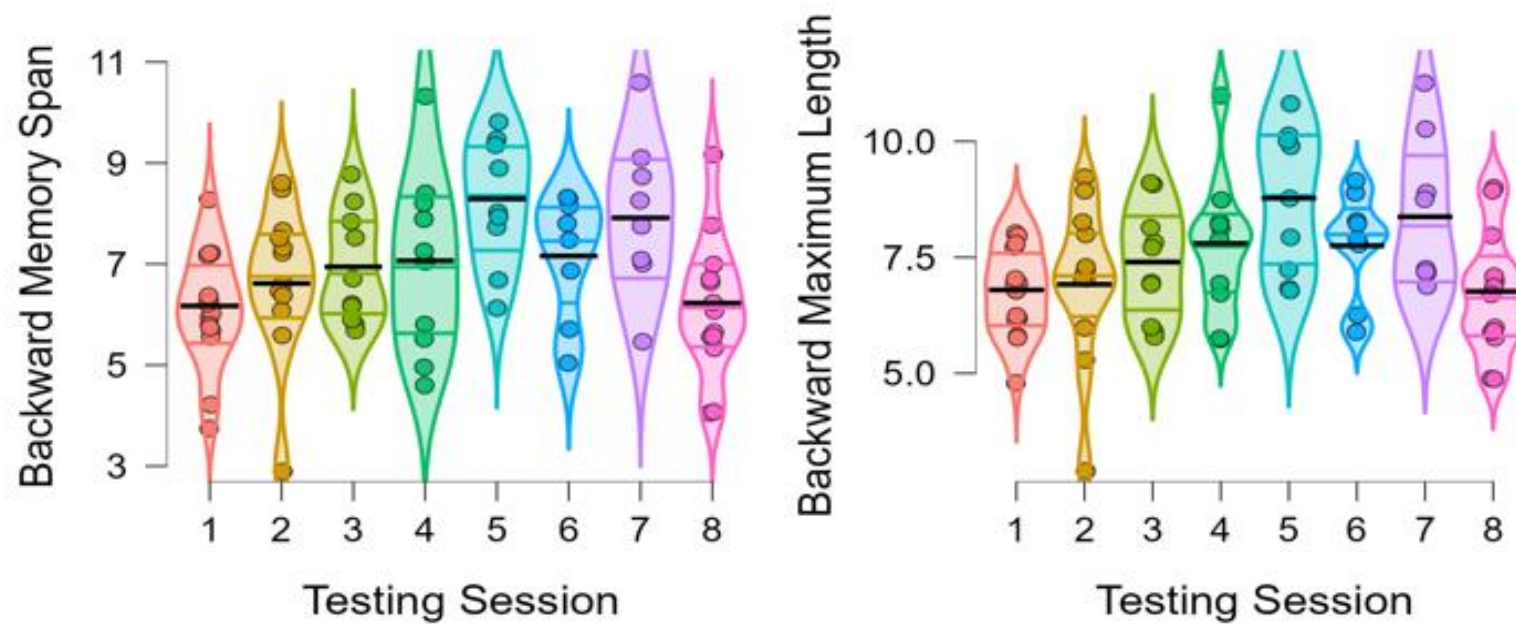


Figure 5.9. Violin plots displaying the distribution of variables Backward Memory Span and Backward Maximum Length across sessions. Scatterplots of individual scores are included in each violin with the black line indicating mean values.

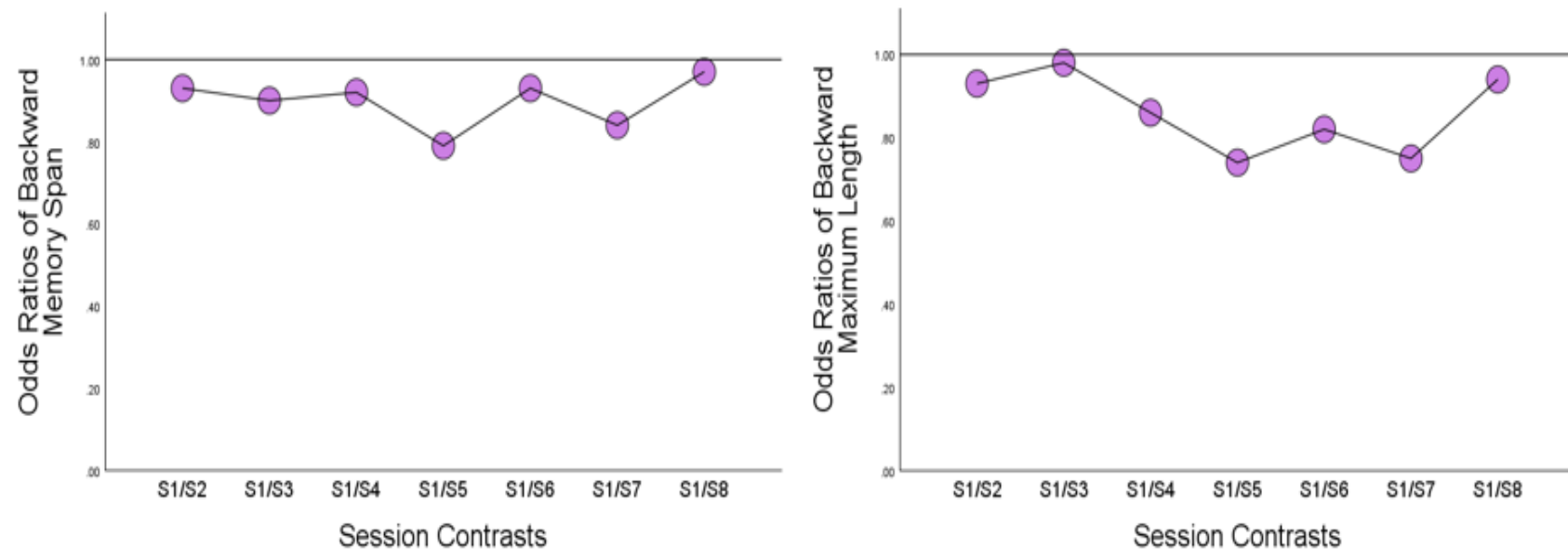


Figure 5.10. Plots of odds ratios of variables compared to baseline indicated relative test stability between baseline and consecutive sessions. Odds ratios in sessions 2 to 8 are slightly below 1 indicating slightly greater BMS and BML scores, representing better memory performance in post-baseline sessions suggesting a small effect of practice.

5.3.7.3. Go/ No-Go

A Bayesian Gamma regression model was used to examine the dependent variable time taken to complete the Go/No-Go test with session as the primary predictor and age, migraine type, and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from this model indicated an effect of Session 2 (24 hrs after migraine 1; 95% CrI = [-0.18, -0.01]), Session 3 (48 hrs after migraine 1; 95% CrI = [- 0.19, - 0.01]). and Session 4 (24 hrs after migraine 2; 95% CrI = [- 0.19, -0.01]) compared to Go/ No-Go test time in the reference level, session 1 (baseline). Pairwise comparisons revealed increased session duration in session 1 compared to sessions 2, 3, 4 and 8 (see Table 5.24).

Table 5.24. Pairwise comparisons of Go/ No-Go completion time between sessions. Statistical effects were determined by 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 24hrs after Migraine 1 (Session 1 / Session 2)	1.100	1.008	1.20
Baseline / 48hrs after Migraine 1 (Session 1 / Session 3)	1.102	1.006	1.20
Baseline / 24hrs after Migraine 2 (Session 1 / Session 4)	1.104	1.005	1.20
Baseline / Baseline 2 (Session 1 / Session 8)	1.088	1.000	1.18

A Bayesian Beta regression model was used to examine the dependent variable combined error rate (both omission and commission errors) with session as the primary predictor and age, migraine type, and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results indicated no effect of combined

error rate and session levels. Pairwise comparisons revealed reduced combined errors in Session 2 (24 hours after migraine 1) compared to Session 3 (48 hours after migraine 1; 95% CrI = [0.083, 0.753], MR = 0.33).

A Bayesian Beta regression model was used to examine the dependent variable total omission error rate with session as the primary predictor and age, migraine type, and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model suggested that there were no effects of commission errors in session 1 and all other session levels. Pairwise comparisons revealed reduced omission errors in Session 2 (24 hours after migraine 1) compared to Session 3 (48 hours after migraine 1; 95% HPD CrI = [0.112, 0.988], MR = 0.404).

A Bayesian Beta regression model was used to examine the dependent variable total commission error rate with session as the primary predictor and age, migraine type, and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model suggested that there were no differences in commission errors across sessions. Pairwise comparisons revealed reduced commission errors in Session 2 (24 hours after migraine 1) compared to Session 3 (48 hours after migraine 1; 95% HPD CrI = [0.087, 0.82], MR = 0.34).

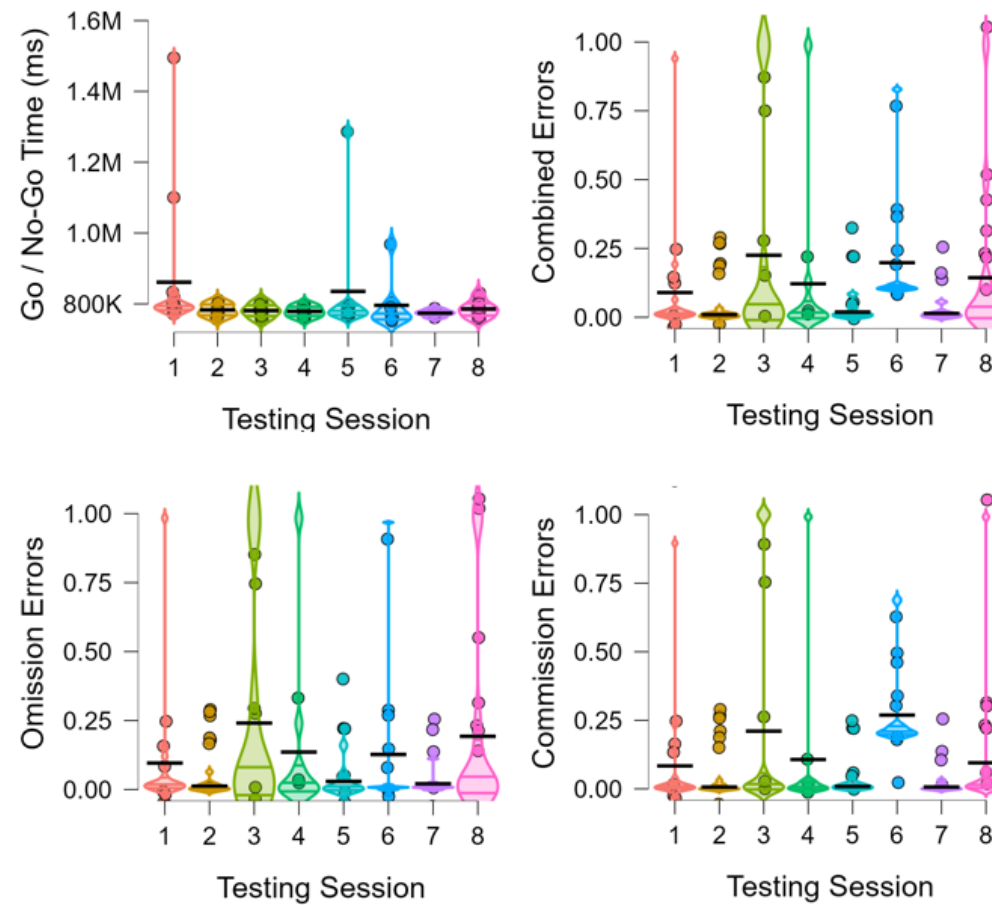


Figure 5.11. Violin plots displaying the distribution of Go/ No-Go scores across sessions. Scatterplots of individual scores are included in each violin with the black line indicating mean values.

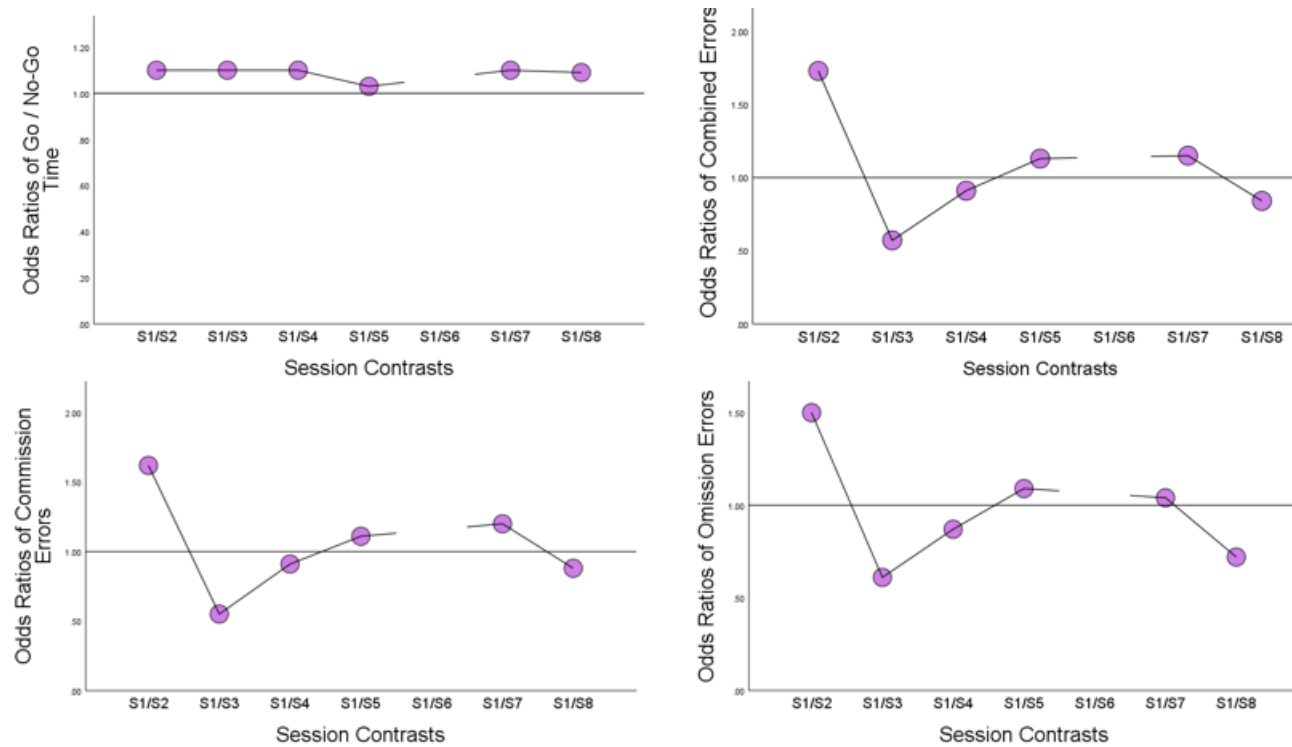


Figure 5.12. Plots of variable odds ratios compared to baseline indicated relative test stability of the variable Go/ No-Go task duration. Error variables were slightly higher in baseline than in session 2. Slight increases in total errors were observed in tests 3, 4 and 8. Error variables (total, commission, and omission) in Sessions 5 and 7 were considerably stable compared to baseline.

5.4. Discussion

The aim of the present study was to clarify the symptomatic and temporal profile of migraine. To do this, a longitudinal, within and between participant approach was used to record the behavioural functioning of a sample of Irish female participants with migraine across a 90-day period. The study aimed to examine the influence of behavioural factors on migraine onset and to characterise behavioural and psychological associations within migraine phases. The findings of the present study identified associations of fatigue, stress, appetite changes and changes in subjective thermal sensation with migraine onset which is consistent with previous studies (Goadsby et al., 2017). Fatigue was also associated with migraine characteristics of severity and duration. The lagged models however returned no significant associations, however, suggesting that the temporal organisation of the prodrome (24-72 hours prior to migraine headache) needs to be reduced in future studies. In the same regard, a number of phase associations that were observed in Section D, such as the sleep timing variables, were marginally significant and as such the clinical value of these associations is questionable. In this section, Sleep Inertia displayed the most interesting results regarding migraine pathophysiology, with associations of increased Sleep Inertia in the prodrome, migraine and postdrome compared to interictally. Finally, no clear pattern in cognitive functioning between interictal assessments and 24- and 48-hour postdrome assessments was observed in Section E. Irrespective of the findings, the present study provides a novel contribution to the literature by highlighting the potential for future research to consider similar longitudinal, multi-modal data collection methods and suitable analytic approaches to handle similar datasets. The present study further highlights

this approach as an effective design to capture functioning in sporadic conditions such as migraine.

In section A, Bayesian models with horseshoe prior shrinkage were used to identify statistically supported predictor variables for migraine onset (excluding highly correlated variables). From these models, the favoured model (Model 10) used a reduced data set that excluded variables with 10% missing data and accounted for individual variance using a random intercept for participant ID. The results suggested that having an unusually increased appetite, unusually decreased appetite, being unusually cold with increased self-reported levels of fatigue, and stress statistically affected migraine onset. However, when the data set was reduced and lagged to include only data from 24-, 48- and 72-hours prior to migraine onset in section two to investigate the prodromal functioning, no predictors were observed. From this, it may be inferred that the significant predictor variables observed in section one was not recorded in in the 72 hours prior to migraine onset or at least clean migraine onset, where there were no phase overlaps. A recent study by Schwedt et al. (2025) found that beyond 6 hours after recording a ‘prodromal’ symptom, migraine only occurred in 4.5% of cases, down from 81.5% of cases in the first 1 to 6 hours. These findings from Schwedt et al. (2025) clarify findings from Section B that were based on theoretical understandings of the prodrome occurring up to 72 hours prior to migraine onset. Furthermore, based on the null findings of this section, it is likely that the effect of the variables of increased appetite, reduced appetite, felt cold, increased stress and increased fatigue observed in section one occurred on the day of migraine occurrence although this was not confirmed in the present study. However, the finding of changes in appetite and temperature

regulation support the role of hypothalamic involvement in migraine (Goadsby et al., 2017).

Section C, which examined the effects of the predictor variables on migraine characteristics observed that increased fatigue was also associated with increased migraine duration and migraine severity. It is possible that the relationship between fatigue and migraine severity and duration is bidirectional where increased fatigue is a result of increased migraine duration and migraine severity and migraine duration and severity is increased by fatigue (Seo & Park, 2018). In section four, older individuals in the study experienced less phase related changes in fatigue. It is possible that older participants who may have been living with migraine for longer periods have adapted coping strategies which help to reduce the impact of the condition. Alongside this, research has shown generally increased fatigue in older participants, potentially reducing the difference in fatigue that was observed across phases in younger participants (Hu et al., 2025).

Contrasting that of the literature, few statistically significant findings on sleep timing were observed in the present study. Sleep timing variables such as sleep onset, sleep end and sleep duration were not found to be important predictors of migraine onset and no clear associations of phase were observed. However, the literature is laden with articles emphasising the association between sleep impairment and migraine (Buse et al., 2018; Duan et al., 2018; Vgontzas & Pavlović, 2018). In line with this, in the current study, phase specific differences in self-reported sleep disturbance frequency were observed. Participants in the study reported more sleep disturbances in the interictal phase compared to the prodrome and migraine phases potentially supporting the aggravating potential of sleep impairment and the therapeutic coping mechanism of sleep during the attack

(Alstadhaug et al., 2007). However, no significant associations or differences in self-reported sleep quality or Fitbit Inspire 2 sleep efficacy were observed in relation to migraine onset or phase including between attacks. However, associations with migraine and sleep quality may be limited to cross-sectional studies and may help to explain the findings presented in this study and that of Vygontzas et al. (2021) which observed no associations of migraine with objective or subjective measures when using a longitudinal design (Schumacher et al., 2023). The subjective and objective measures of sleep in the present study were relatively comparable (see tables 4.6 and 4.7). However, in line with research by Vygontzas et al. (2020), participants in this study overestimated sleep timing variables such as sleep onset, end, and duration.

Section E focused on the neuropsychological performance of the participants. The scores from the Trail Making Sessions A & B, Visual Backwards Digit Span and Visual Go/ No-Go were modelled with session as the main predictor variable. Some of the variables from these sessions showed decreased performance 48 hours after a migraine compared to 24 hours after a migraine (Trail A time), which contradicts the hypothesis of temporary cognitive dysfunction that would return to normal with increased time following an attack. However, this trend was not consistent across all 24-hour and 48-hour assessments and although the models and pairwise comparisons returned numerous statistical effects of phase, there was no consistent pattern to performance as expected. Inspection of S1/S8 contrasts which were both interictal sessions suggest that much of the variance observed across sessions was not due to migraine. Rather, inspection of odds ratio plots indicated considerable instability of the Trail Making Test and Go/ No-Go across sessions which may reflect changes in difficulty, practice effects, contextual noise, and general variance in performance although efforts to limit the impact of practice were

applied to the study design. The session stimuli were altered to create new trails (TMT A & B) and stimuli colours (GNG) which may have limited practice but introduced variance in test difficulty across sessions. This may explain significantly improved performance as evidenced by the mean scores in Session 2 denoted on the violin plots above (see figure 5.7). This is a limitation of the study using a repeated measures longitudinal design. The choice of neuropsychological assessments used in the present study was made based on practicality of the tests and the requirements that would be placed on participants recovering from a migraine. It was desired that tests could be done on any device such as a phone or tablet to make the study accessible and kept to a duration of 30 minutes to encourage participation. Tests which were auditory based were decided against to preserve participant welfare as phonophobia is a common migraine symptom that is well documented in the literature (Ashkenazi et al., 2009; Suzuki et al., 2021). As such, the test-retest reliability and effects of practice could have been investigated further during the design process. While studies have further observed sufficient test-retest reliability of the Trail Making Test and Backwards Digit Span, a significant practice effect has been observed particularly for the Trail Making Test (Buck et al., 2008; Scharfen et al., 2018). Due to this, Buck et al. (2018) suggests that considerable time be between assessments and use of distractor elements alongside alternating trails be used for the Trail Making Test. Of the neuropsychological tests used in this study the Backwards Digit Span is documented as being more robust to repeated assessment and practice effects (Scharfen et al., 2018). Although mean performance gradually increases over each of the sessions, the Backward Memory Span measure in particular seems to be sensitive to changes as evidenced by the violin plots of Backward Memory Span which show a pattern of reduced memory performance at 24-hours post migraine

compared to 48-hours post migraine (see Figure 5.9). Contrastingly, significant practice effects on the Go/ No-Go have further been recently documented alongside poor test-retest reliability (Zorowitz et al., 2025). As such, Zorowitz et al. (2025) suggest using a modified Go/No-Go which has shown increased reliability and limited effects of practice. As this study required repeated assessments not only across the span of the study but at 24- and 48-hour intervals there may have been considerable effects of practice on all assessments however it is likely that this effect was greater for Trail Making and Go/ No-Go test performance which rely on time-based measurements.

A review by Munnilari et al. (2023) on performance variability across a single day has found that reaction time may be greater in the evening compared to during the day. Reaction time is intrinsic to the Go/ No-Go test as all stimuli are displayed only briefly and the participant is required to determine a go or no-go cue on the presentation of the stimuli and failure to do so may be recorded correctly as a no-go response or incorrectly as an omission error. The effect of time of day on performance however may be more general and impact a number of cognitive domains with peak performance being determined by individual chronotype (Wiłkość-Dębczyńska & Liberacka-Dwojak, 2023). As such, it is recommended that individual chronotype and time of day control assessments be included in future designs (Wiłkość-Dębczyńska & Liberacka-Dwojak, 2023). Future studies may investigate intra-daily measurements of potential prodrome symptoms.

The findings of this study emphasise migraine beyond the misconception as a pain disorder. Across the migraine phases, numerous changes in psychological and physiological functioning can be observed. The statistical effect of hypothalamic, homeostatic behaviours such as appetite changes and temperature regulation on

migraine onset was observed in Section A. This coupled with the phase level differences in sleep behaviour highlight the potential role of homeostatic processes in migraine pathophysiology and warrants further investigation to determine any causal relationships between hypothalamic behaviours and migraine (Goadsby et al., 2017). The cognitive impact of migraine is less clear and the findings from this study highlight the methodological difficulties associated with research into the disorder. However, it is hoped that future research may consider the nuances of the present study during the research design process.

In that regard, there are several limitations of the present study. Although there were a substantial number of observations, the sample was small and consisted of 15 female participants, future studies may aim to replicate the study's procedure with a larger sample that is sex balanced. Alongside this, as this study was not in association with a headache clinic, the sample consisted of self-reported diagnosis of primary migraine by a licensed medical practitioner which may have consisted of incorrectly diagnosed or self-diagnosed participants. Another substantial limitation with the present study is the effect of practice on repeated measure neuropsychological assessment. Future studies may investigate the potential of using varied neuropsychological assessments with high construct and criterion validity to counteract the effects of practice associated with repeated assessments and to enable clearer comparisons of postdrome cognition. As well as this, due to the burden associated with the neuropsychological assessments, it would be valuable for patient and public involvement in the research design process to choose assessments that are associated with less burden and account more for the potential impact on participants with sensory symptoms such as those observed in migraine (Aiyegbusi et al., 2022; Mes et al., 2019; Suzuki et al., 2021). This study further failed to account for several

potential confounding factors that implicate health and behaviour. As such, future research should also aim to replicate the present study while controlling for the effects of confounding factors such as but not limited to, racial/ethnic identification, education, income and socio-economic status, body mass index, caffeine intake, alcohol intake and tobacco use which further limit the generalizability, reliability and interpretation of the findings (Darmon & Drewnowski, 2008; Giskes et al., 2010; Grandner et al., 2010; Patel et al., 2010).

The study also has several strengths. For example, this study may act as a prototype as a successful research design to examine behaviour and cognition in sporadic disorders such as migraine. Furthermore, the participants in the study were enthusiastic to take part. The methods used in the study were successful as measured by the engagement. Participants completed the daily diary and wore the Fitbit Inspire 2 devices for the duration of the study. Furthermore, the remote neuropsychological assessment was successful with good uptake even though there is significant burden associated with the assessments (Howieson et al., 2019).

With respect to the theoretical frameworks employed in this thesis, the present study reinforced the findings of Chapter Three and Chapter Four that hypothalamic based regulatory behaviours such as sleep and eating behaviours are implicated in migraine (Giffin et al., 2003; May & Burstein, 2019; Schulte & May, 2016). In this chapter, the findings of the phase analyses in Section C and Section D suggest the potential need to refine the temporal window of the prodrome and postdrome phases, as very few associations were observed, contrasting that of previous research (Giffin et al., 2003; Goadsby et al., 2017; Kelman, 2004; Schwedt et al., 2025). Regarding circadian rhythms in migraine, the present study highlights the need to refine their investigation using similar designs by including assessments

to determine and account for alternate determinants of sleep timing such as work and social factors (Golombek & Rosenstein, 2010; Roenneberg et al., 2003; 2019). Sleep timing and duration may remain relatively unaffected despite underlying circadian physiology, and circadian misalignment may instead be reflected in physiological and behavioural outputs that were not assessed in this study, such as dim light melatonin onset or meal timing (Benkli et al., 2023; Golombek & Rosenstein, 2010; Pot, 2018). Separately, it is also possible that circadian misalignment is limited to specific phases, indicating the need to refine the temporal window of the phases beyond the 24-72 hour window used in the present study (Schwedt et al., 2025).

The present study highlighted the presence of non-painful migraine symptoms including fatigue, appetite changes, stress and changes in perceived body temperature. These symptoms, which are commonly reported as part of the migraine prodrome, are often overlooked by pharmacological approaches to treatment. As such the present study furthers the argument for the inclusion of psychological treatments in migraine to target these non-painful symptoms. The present study further highlights the difficulties of researching migraine. For example, migraine phases may overlap, leading to questions around how this should be handled in research. Similarly, to investigate sporadic cognitive impairment in migraine, consideration must be given to neuropsychological measures with high test-retest reliability due to the need to have repeated measure designs.

Chapter Six

“I thought I would do this; I’m giving my 10-pence worth.”: Thematic Insights from Participants Research Experiences.

Abstract

Research designs which avail of longitudinal observation or time-consuming, abstract tasks such as neuropsychological assessment can be particularly burdensome on participants (Davis et al., 2002). As such it is important to get participant feedback or patient-public involvement in the research design process to limit the negative impact of research participation on participants. The present study used semi-structured interviews to gain insight into the experience of 10 individuals with migraine who took part in a longitudinal study that lasted 90 days and required daily participation and repeated neuropsychological assessment. All transcripts from the interviews were analysed using thematic analysis. Results from this study indicated three overarching themes in the data, positive experiences, negative experiences and feedback. Overall, participants were eager and happy to contribute to research that may potentially benefit them in the future and found that daily recording of their migraines enabled greater insight into their condition. Some burden was associated with the duration of the study and daily participation became more burdensome over time. However, the neuropsychological assessments were the most burdensome aspect of participation. This study concluded that overall, participants were happy to take part in research that was seen as improving the understanding of their condition. The findings from this study highlighted the need for careful consideration when considering neuropsychological assessment in individuals with migraine. Furthermore, the findings highlight the importance of incorporating patient and public involvement (PPI) throughout the research design process to ensure the research methods acknowledge the needs and preferences of individuals with migraine.

6.1. Introduction

One of the major limitations of migraine research is the spontaneous nature of the condition, which makes capturing the attack in research difficult (Goadsby et al., 2017). Although migraine may be induced pharmacologically, the induced migraine is not fully comparable to that which occurs naturally in the disorder (Ashina et al., 2022). Another limitation is that there is significant variance between and within individuals with migraine; not all individuals with migraine experience the same symptoms and not all migraines are the same within the same individual (Kelman et al., 2004; Viana et al., 2016). As such, there is a clear need for longitudinal designs in migraine research that enable multiple observations within and between participants (Gao et al., 2024). This study design can be particularly burdensome for participants as it requires a significant amount of time and effort across the duration of the study (Davis et al., 2002). Furthermore, through understanding the experience of participants, improvements can be made to future studies encompassing similar designs (Teague et al., 2018). Following completion of the longitudinal study described in Chapter Five, participants were asked if they would like to participate in the qualitative interview study outlined in Chapter Four. As part of the semi-structured interviews participants were asked some questions on their experience participating in this longitudinal study. The present study aims to summarise the experiences of the participants who took part in the longitudinal study as a means to guide future research availing of similar methods.

6.2. Methods

6.2.1. Participants

Non-random purposive sampling was used. Participants who were interested in taking part in the longitudinal study described in Chapter Five, were asked to email the researcher expressing interest in participation. All individuals were screened regarding the inclusion criteria. If eligible, participants were asked to provide their home address to post out study materials for the longitudinal study alongside information and consent sheets which had to be signed and returned by post to the Department of Psychology, Maynooth University. The information and consent sheets included details of both the longitudinal study and the qualitative study outlined here and in Chapter Four. It was hoped that using one sample of participants for all studies would enable a comprehensive understanding of their migraine and enable critical feedback on their experience participating in the previous longitudinal study. Following completion of the longitudinal study, participants were emailed asked if they would still like to take part in semi-structured interviews that aimed to capture the subjective experience of migraine that was not considered in the longitudinal study. The inclusion criteria for participating were those of the longitudinal study and included the following: (1) individuals were required to be at least 18 years old and able to provide informed consent; (2) they had to have daily access to the internet; (3) a professional diagnosis of primary migraine was required, with neither a secondary health condition that may be causing their migraine, nor a history of psychiatric treatment and diagnosis. Moreover, due to the nature of the previous study it was also required that (4) participants were a resident of the Republic of Ireland. The ten participants who took

part in the study were all female with ages ranging from 32 to 63 years, with the mean age being 43 years. Of these participants, six were diagnosed with migraine without aura and four were diagnosed with migraine with aura, two of whom occasionally experienced migraine without aura. For the purpose of the analysis, participants were given numbers to maintain anonymity (Participant 1, Participant 2 ... Participant 10).

6.2.2. Data Collection

All participants were asked for consent before participating, which included consent to record the audio of each interview to enable transcription. Interviews were conducted online using Microsoft Teams between December 2023 and May 2024. As part of the interview process described in the previous chapter, questions were included to capture the experience of participating in the longitudinal Fitbit study described in Chapter Five. The interview schedule for this section is outlined in table 6.1. The audio from each interview was recorded and automatically transcribed using Microsoft Teams. The researcher then listened to each interview with reference to the draft transcript to ensure accuracy. An orthographic transcription method was used to generate a detailed verbatim account of each interview, including both speech and non-verbal vocalizations.

Table 6.1. The interview schedule regarding experience participating in the current study.

I would now like to just ask you about your experience participating in the previous 90-day Fitbit study.

- 1. What did you think of the study?**
 - 2. How did you feel about your participation in the study?**
 - 3. Were there any aspects of the study that you found challenging?**
 - 4. Did participating in the study have any impact on your physical or emotional wellbeing? If so, can you please explain.**
-

6.2.3. Analysis

The analytic procedure began as outlined by Braun and Clarke (2006; 2019) with the familiarisation of the interview data. During this stage, the researcher read the transcripts and made notes of key points of interest, such as recurring topics. In this stage, it was also important to consider the meaning behind the data (Braun & Clarke, 2006; 2019). Each interview was read in full a minimum of two times during the familiarisation stage. Following the familiarisation stage, the researcher began reading through each of the transcripts and identifying segments that were relevant to the research question or of particular interest. The qualitative software MAXQDA was used to accumulate and keep track of recurring codes in the transcripts. This approach to coding is best described as *complete coding*, as the approach was more

general and open than, for example, selective coding, which has very clearly defined topics of interest (Braun & Clarke, 2006; 2019). Codes were written to be concise and capture the important information and interpretation of the data. Some segments of the data included multiple codes. When each interview had been coded, the codes were revised and considered with regards to the interview segments they captured and whether codes were linked to each other and could be grouped together to depict a more nuanced theme or pattern in the data. Once themes had been developed, it was necessary to review the coded segments and ensure that the themes accurately reflected the coded data. Once themes were finalised, they were written up with reference to segments from interview transcripts to illustrate the experience of the participants. This analytic process was not linear, and each step was revisited multiple times, with various proposed codes and themes discarded or edited throughout the writing process.

6.3. Results

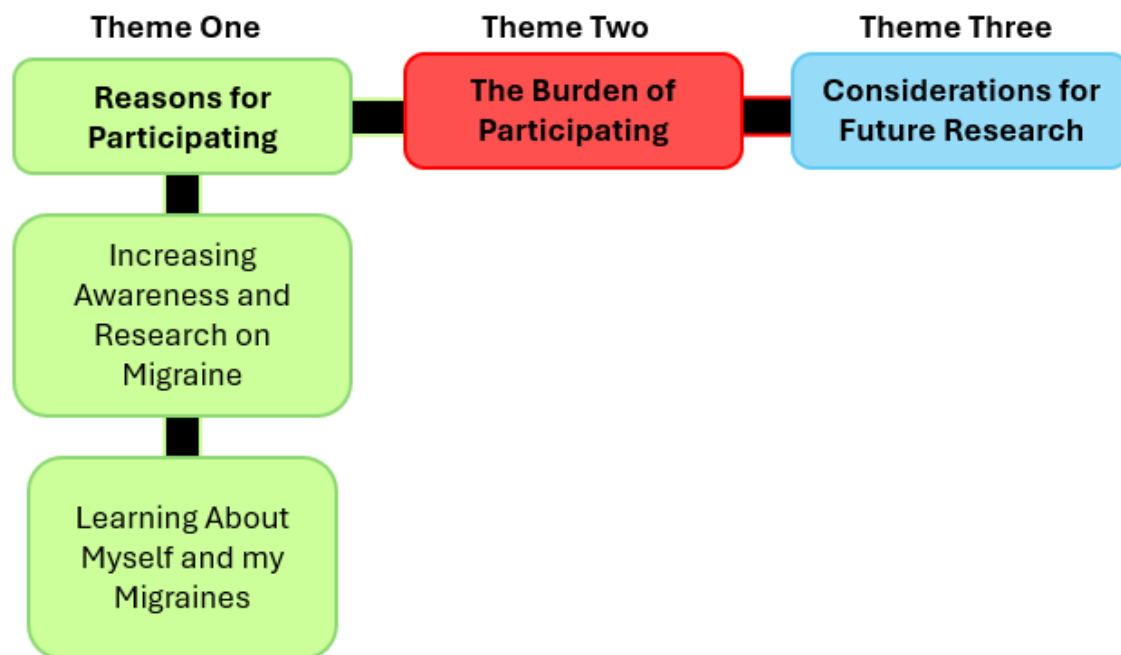


Figure 0.1 Thematic map of the themes presented in this study.

Reflexive thematic analysis was used to convey the participants responses when asked about their experiences participating in the study. From the analysis, three themes emerged: *Reasons for Participating* (n= 9), *The Burden of Participating* (n=6), and *Considerations for Future Research* (n= 4). The first theme, *Reasons for Participating*, included two subthemes of *Increasing awareness and research on migraine* and, *Learning about myself and my migraines*.

6.3.1. Theme 1: *Reasons for Participating* (n= 9)

6.3.1.1. Subtheme One: *Increasing awareness and research on migraine* (n = 6)

Many of the participants expressed their interest in participating came from a sense of understanding that “*didn't feel like there was enough research done for, for, for people with migraines, and that it was kind of just seen as a headache*”

(Participant 1). Part of this was also driven by empathy for their peers with migraine and a need to help those who were suffering more from migraine by contributing to research.

“I just feel I want to help the others because, they sound so bad and they're.. like a lot of women, and I just feel, I feel like it's not been taken seriously enough.

...

I thought I would do this. I'm giving my ten pence worth.” (Participant 2)

“Well, the, the way I see it is, I'm contributing to like research into migraines that might help me or others in the future so.” (Participant 4)

One participant commented on the aims of some of the research as being a motivating factor for participating:

I thought it was very novel and I really liked the fact that, you know, part of it was looking at, I don't know if this is the right word, but at the cognition and the ability to perform tasks because I think that's something that's really forgotten, not forgotten about, but it's not recognised by others, you know, in the general public. It's not necessary that, I mean, it's recognised amongst the specialists and the doctors, you know, they say we know it's affecting you, but it's not, you know, medications, treatments are not aimed at that.
(Participant 10)

6.3.1.2. Subtheme Two: Learning about myself and my migraines (n= 7)

Another benefit that was consistently reported by the participants was that participating in the longitudinal study enabled them to look at their behaviour and identify potential triggers for their migraines.

“I suppose it just educated me a bit more on what I was doing or what I needed to do more of I suppose or less of. It made me more aware of triggers or patterns involved I suppose.” (Participant 1).

“Like, I definitely found that, like, I know my other triggers is like, if there's a lot going on emotionally or if there's a lot going on.” (Participant 5)

The diary and Fitbit aspect of recording behaviour every day was also useful to some participants as it helped them gather information to provide to their neurologist.

“I suppose it helped me to gather just a bit of data about my migraines 'cause I never really got that organised to do that.” (Participant 6)

“The study actually directly helped me was I was able to consolidate and like say I suppose, research my sleep pattern and I then was able to actually bring it into my neurologist.” (Participant 8)

For one participant, reviewing their activity each day enabled them to reflect on their migraine experience as they previously thought that they had to maintain a strict routine. However, upon reviewing their data they were able to see that when they deviated from the routine there was no impact on their migraines.

“I think there was a bit of reassurance in that go well, actually look at all this. I'm keeping track of this and actually I haven't been any worse and yet I can see in black and white.” (Participant 9)

For another participant, being able to see their day-to-day behaviour enabled them to pinpoint areas that they needed to work on generally such as sleep duration each night: *“Yeah, I actually also found it encouraging to help me have a better sleep duration. So, it's good to go to bed earlier. It encouraged me to go to bed earlier, which I'm not great at.” (Participant 10)*

6.3.2. Theme Two: The Burden of Participating (n= 6)

In terms of more negative experiences associated with participating, some participants spoke of the difficulties of keeping up with the study's requirements such as filling out the diary every day or syncing the Fitbit.

“...reminding myself to make sure I had downloaded the watch to my tablet, just making sure every day I had synced it.” (Participant 8)

“I suppose I probably struggled with my forgetfulness more than anything.

Yeah. So that was it, just making sure that I'm keeping track.” (Participant 6)

For one participant, the burden of participating was more noticeable in the third month of the study.

It was totally grand. It was the last couple of weeks. I found myself kind of, you know, not doing it right away and kind of leaving it a little while and then being crossed myself for doing that. Do you know what I mean? Not writing it down. (Participant 5)

Two participants spoke of the Fitbit being uncomfortable to wear for a long time.

“I found it really hard to keep the watch on my hand all the time. I felt like I was nearly... like it nearly I felt like I had to get it off.” (Participant 5)

“I didn't find it particularly comfortable to wear while sleeping.”

(Participant 10)

Two participants also spoke about the neuropsychological assessments. One participant found that they triggered an attack:

“I really struggle cognitively trying to complete them tasks like my brain, my brain wouldn't let me. I remember I tried to do one day, one of them one day and my head started hurting halfway through.” (Participant 8)

While the other participant found that the assessments made them feel nauseous,

“when I was doing them post migraine, even those 24 hours or 48 hours, I actually felt like quite nauseous doing them, like, really nauseous. (Participant 7)

Both participants mentioned that this was mostly in reference to the Go/No Go test.

Two participants spoke of the Fitbit being inaccurate for recording sleep duration, as it recorded when participants might have been just lying down as being asleep.

“I just went to lie down. But the Fitbit would count it as sleep and say, oh, you've got 10 hours sleep last night.” (Participant 1)

*“This would say you'd slept for 8 hours or something... And I did in my **** sleep for 8 hours.” (Participant 7)*

6.3.3. Theme Three: Considerations For Future Research (n= 4)

Some participants also gave feedback on how participation may be improved if the design was to be utilised again. One point that was made by two participants was that a small qualitative piece should be included in the diary, for participants to add information that wasn't included in the diary such as making note of

menstruation occurring or whether they took medication: “*So maybe even if there was like a little section where you could put in, you know, did you or not, did you not take medication?*” (Participant 4). Participant 4 also said that an online format could also be used to make participation easier; “*I think maybe even like if it was like an app where you could fill out a, a quick form online.*”

Two participants also spoke that they found it difficult to keep track of the neuropsychological assessments, as it wasn’t possible to predict whether they would get an attack the next day which would potentially skew the results.

“*You know, the way we do the tasks 48 hours after the end of a migraine. So, I could do that task at the end of that migraine, but theoretically I could be starting another migraine. Now. I tried to avoid doing that. You know what I mean?*” (Participant 10)

6.4. Discussion

Following analysing the data, three themes were generated from the data; *Reasons for Participating*, *The Burden of Participating* and *Considerations for Future Research*. Of these themes, *Reasons for Participating* was the most frequent theme in the data. This theme further had two subthemes: *Increasing awareness and research on migraine* and *Learning about myself and my migraines*. The first subtheme *Increasing awareness and research on migraine* was encapsulated by participants in the study who frequently mentioned being happy to help with research into migraine, a condition which they felt was under-represented in research, partially because of their own experiences with migraine, particularly the non-painful symptoms of the condition which aren’t the focus of treatment (Syn et al., 2023). This is line with research which observed that people were more likely to take

part in research which is of perceived personal benefit (Nappo et al., 2013; Syn et al., 2023).

The second subtheme, *Learning about myself and my migraines* was more specific to the design of the longitudinal study which utilised daily diary entries and wearing a Fitbit device. By the end of the study period, participants noted that they were able to use the data they recorded for insight into their migraines. Some participants were able to give the data to their neurologist or general practitioner as this level of recording is advised by national health boards such as the National Healthcare Services to clinicians, as a means to guide treatment decisions (Jonker et al., 2022). Participants noted that they had never managed to keep track prior to the study. Furthermore, being able to see their data each day, was reassuring for some participants who noted that they didn't have to be so strict with their routine, or for others it highlighted the need to improve their routine, such as by getting more sleep. The clinical utility of tracking in migraine is emphasised in studies such as Raffaelli et al. (2022) which observed that adherence to an electronic diary reduced the frequency and severity of migraine attacks. These findings further highlight the utility of self-management in migraine through the SEEDS framework (sleep, exercise, eat, diary and stress), whereby the diary can be used to examine these factors at baseline along with medication use and attack frequency (Roblee & Starling, 2019).

The theme *The Burden of Participating* highlighted the general burden associated with long-term participation, and the nature of participation as being an active daily action rather than passive. As time went on, the more effort was required to participate, and participants noted their adherence to the studies requirements waned. This is in line with existing research on sample retention (Davis et al., 2002).

A more specific burden of the present study however was wearing the Fitbit device continuously as it became uncomfortable for some participants.

The most concerning burden associated with participating, however, was regarding the neuropsychological assessment aspect of the study. As some participants noted, they found the neuropsychological assessment particularly triggering for their migraine during the postdrome period and caused their head to start hurting again or caused feelings of nausea. This may be partially explained by the tasks being performed remotely on devices such as a smartphone or computer; which is often referred in research to be particularly triggering coupled with the sensitivity to light that is characteristic of the condition (Schwedt, 2013; Roy et al., 2024). Furthermore, the Cued Go/No-Go task flashes the cue without colour before flashing the coloured go or no-go stimuli, this could further worsen symptoms in individuals during the post-drome (Millisecond Software, 2022). Based on these findings, the Go/No-Go test should be avoided where possible however more research is needed to establish the impact of other neuropsychological assessments on individuals with migraine. Further consideration should be given to the use of remote versus in-person neuropsychological assessments with patient-public involvement, as although remote assessment provides convenience particularly where migraine is unpredictable but also increases the exposure to artificial light from screens. However, attending in-person assessments during the migraine headache and post-drome phases may not be feasible due to the travel requirements and may be particularly strenuous when in pain or recovering from pain.

The theme of *Considerations for Future Research* was the less frequent across the interview data. Minor changes to the study design were proposed such as converting the daily diary to an online format over paper format which may make

daily adherence easier. This was considered however paper format was preferred to limit screen exposure, and it was believed that having a physical copy of the diary would act as a cue to continue participation. Furthermore, it was observed in the longitudinal study that participants who made it until the first 30-day marker of the 90-day study, completed the study in full. However, frequent communication was kept with the participants throughout the study duration which has been shown to impact sample retention (Davis et al., 2002). So, it is not clear whether the physical diary or online diary would be preferred for sample retention and ease of participation in future research.

The present study highlights that although there are some burdens associated with participation in intensive research such as those with daily measurement and longitudinal designs, some factors may help to encourage sample retention. In this study, participants spoke of a sense of purpose associated with contributing to migraine research and care with a sense of benefitting personally from participating. Not only did participants indirectly benefit from the research output but the method of recording their migraines, sleep and activity. Alongside this, the themes associated with participation burden and feedback for future research emphasise the importance of patient and public involvement in the research design process, to create projects which fully consider the lived experience of the target population.

Chapter Seven

General Discussion

7.1 Introduction

The primary aim of this thesis was to investigate migraine as a cyclical neurological disorder with biological, psychological, behavioural, and social manifestations. The conceptual foundation of this research draws on multiple related but distinct bodies of literature. The first is the chronobiological framework, which emphasises the temporal organisation of biological processes and behaviours such as activity, sleep and eating (Benkli et al., 2023; Roenneberg et al., 2019). The second framework concerns contemporary migraine research suggesting that sleep and feeding disturbances may not act entirely as external triggers or aggravating factors but represent manifestations of an early phase of the migraine attack—the prodromal or premonitory phase (Karsan & Goadsby, 2018). This understanding further suggests a postdrome phase following the migraine pain where the individual experiences cognitive difficulties among other symptoms (Bose et al., 2018). In this regard, migraine is cyclical, with symptoms beginning in the prodrome phase and returning to normal following the prodrome. A central question of this thesis was if migraineurs are particularly susceptible to circadian misalignment, as reflected in their sleep and dietary behaviours, and whether this associated with increased migraine frequency. The following chapter will act as a general discussion for the empirical chapters within the thesis. This chapter will summarise the findings of the thesis and situate them within the theoretical framework. Finally, the implications, limitations and strengths of the present research will be discussed.

7.2 Summary of the Findings Presented in this Thesis

In recent years, cognitive symptoms have been described as a feature of the migraine attack, particularly the postdrome following the headache stage. For this reason, in Chapter Two we conducted a scoping review of the literature on cognitive functioning in individuals with migraine. Using PRISMA guidelines for systematic reviews, 1742 studies were screened blindly against the inclusion criteria which required studies be conducted in an adult sample aged 18 years or older and use standardised objective measures of cognition. Following the screening process, 57 studies were included in the review. The findings of the review were heterogeneous with some studies reporting significant cognitive deficits in individuals with migraine between attacks in comparison to controls while others observed no differences. The studies observed significant impairment cognitive domains of perception, attention, memory, visuospatial and executive functions. The findings of the review suggested that visual and auditory perception are impaired in migraineurs with a notable discomfort due to visual tasks (Agessi et al., 2014; Chu et al., 2011; Koppen et al., 2011; Zhang et al., 2012). Across attention tasks, migraineurs typically displayed impaired attention and information processing speed (Agessi et al., 2014; Gil-Gouveia et al., 2015; Martins et al., 2012; Mickleborough et al., 2013; Ferreira et al., 2018; Poormina et al., 2017). Studies investigating memory suggested impairment of various memory processes (Agessi et al., 2014; Gil-Gouveia et al., 2015; Santangelo et al., 2016; Tunç et al., 2018; Santos-Lasaosa et al., 2013) including general free recall and recognition (Gasbarri et al., 2008), long-term memory (Raimo et al., 2022), visuospatial memory (Baschi et al., 2019; Huang et al., 2017) and verbal memory tasks (Kim et al., 2020; Latysheva et al., 2019; Lo Buono et al., 2019). Deficits in executive function were observed in terms of slower set

shifting and cognitive flexibility (Han et al., 2019; Lo Buono et al., 2019; Pellegrino-Baena et al., 2018; Poormina et al., 2017; Schmitz et al., 2008; Yannick et al., 2015), impaired decision making (Biagianti et al., 2012; Viticchi et al., 2017), worse performance in working memory tasks (Ferreira et al., 2018; Santos-Lasaosa et al., 2013), and impaired prospective memory (Santangelo et al., 2018). When taken together the findings from the scoping review highlighted the lack of consensus on cognitive measures used in migraine research. This impacts the ability to accurately characterise the neuropsychological profile of the condition as different measures of cognitive domains are not easily compared and a discrepancy in results was noted between studies. Similarly, there was a lack of longitudinal studies that investigated phase-specific functioning, that is, cognitive performance at different phases of the migraine attack; the prodrome, headache, postdrome and between attacks. This is a major limitation to neuropsychological research as this is needed to establish if impairment exists, is it specific to certain phases. This particular limitation informed the inclusion of postdrome neuropsychological assessment in Chapter Five. An update to the scoping review was completed to include studies published following publication up until the submission of this thesis. The update indicated that the research began to recognise the need for longitudinal designs in migraine research. However, with that came new difficulties associated with repeated neuropsychological testing and the effects of practice. This study has been published and is openly accessible through the following link: <https://doi.org/10.1002/ejp.2244>.

In Chapter Three, the associations between sleep and eating factors in individuals with migraine and non-migraine controls were investigated. In particular, sleep factors such as sleep timing, sleep duration, sleep quality and eating factors such as self-regulation of eating behaviours as a means to understand the potential

circadian associations with migraine that have been previously described in the literature (Benkli et al., 2023). Prior research investigating circadian features of migraine have not investigated eating behaviours or self-regulation of eating, although many individuals with migraine report eating behaviours such as fasting or eating certain foods as aggravating factors for migraine (Kelman, 2007). The results of this study found no significant differences for circadian variables of sleep timing. However, significant differences in weekly and workday sleep duration were observed with individuals with migraine sleeping longer than individuals without migraine. Individuals with migraine also displayed significantly reduced food fussiness, greater hunger and reduced self-regulation of eating. All of these factors excluding hunger were found to be significantly associated with increased odds of having migraine. Further examinations of within migraine frequency groups also showed significant differences in food fussiness with individuals who have less than one migraine a month displaying reduced food fussiness than those who have 1-14 migraines per month. The absence of significant differences in circadian variables in this study raised questions on the suitability of cross-sectional data collection to examine migraine as a sporadic condition. It was possible that changes in circadian variables would not have been detected using a cross-sectional design. This potential limitation was important in informing the longitudinal study design employed in Chapter Five. This study has been published and is openly accessible through the following link: <https://doi.org/10.1080/07420528.2026.2620509>.

In Chapter Four, we were able to understand the subjective lived experience of migraine using thematic analysis to compile themes in data obtained from semi-structured interviews. This study was included in recognition that objective measures and the subjective lived experience of migraine do not always fully align, and

reliance on objective assessments alone may provide an incomplete understanding of the condition (Buse et al., 2021). Accordingly, we sought to avoid reducing participants' experiences to objective measures alone by incorporating a qualitative component, thereby capturing aspects of migraine that may not be adequately reflected by quantitative approaches (Buse et al., 2021). The interview schedule also mirrored some of the key questions examined in the other empirical chapters around non-painful symptoms that occur prior to and following a migraine headache, in the prodrome and postdrome phases. The findings from this study emphasised the biopsychosocial nature of migraine that goes beyond studies which opt for objective measures. The thematic analysis revealed four themes in the data: *Mental Wellbeing*, *Treatment: Trial and Error*, *Fight for Control* and *Not just a Headache*. In the theme *mental wellbeing*, the psychological impact of migraine was discussed. The participants in the study highlighted the important role of anxiety as a result of their condition. Particularly, not being able to predict the onset or qualities of their migraine was a source of anxiety. Alongside anxiety, participants also struggled with self-conscious emotions of guilt and shame which were also closely related to their migraine experience and the impact of migraine on their ability to function in normative society. *Treatment: trial-and-error* was the second theme in the data. Here participants spoke of the difficulties associated with migraine treatment, such as trialling medications and dismissive experiences with medical professionals. The theme *fight for control* emphasised the constant back and forth between trying to control the impact of migraine by trying to prevent it with medication and lifestyle changes or controlling the pain with acute medication and the loss of control when the migraine inevitably occurs and doesn't respond to medication. The final theme, *not just a headache* highlighted the variety of symptoms associated with migraine

aside from the headache. Participants spoke of affective, physical, and psychological symptoms. Such symptoms are not widely recognised by individuals without migraine, often creating a lack of understanding and stigma by others particularly those in the wider community. This specific theme had some overlap with the findings of Chapter Two and Chapter Five as participants recalled some non-painful effects of migraine. It was expected that the experience of prodrome and postdrome symptoms would take up a more substantial part of the interview and subsequent analysis but as noted in Chapter Four, participants experienced difficulty in recalling these symptoms which are often very ordinary in nature (Giffin et al., 2003).

Chapter Five utilised a longitudinal design to measure daily self-reported mood, stress, fatigue, and sleep timing behaviours alongside Fitbit actigraphy data on sleep, activity, and heart rate. Alongside this, neuropsychological functioning was assessed during the migraine free interictal period and during the postdrome period following three migraine attacks. This chapter was largely informed by the scoping review in Chapter Two and the cross-sectional study in Chapter Three. These chapters highlighted a discrepancy in migraine research, in terms of not assessing phase-specific behavioural factors as well as neuropsychological functioning. The results of this study were organised into six sections. In Section A, Bayesian multinomial modelling was used to assess which independent variables affected migraine onset. Findings from these models observed that appetite changes, feeling unusually cold, fatigue, and stress statistically affected migraine onset. In Section B, 24-, 48- and 72-hour lags were applied to the independent variables and were used to model migraine onset as the dependent variable; however, no associations were observed. In Section C migraine characteristics such as pain severity, migraine duration and time of migraine onset were modelled. Results from these models

indicated that increased fatigue was associated with increased migraine duration and increased pain severity. Decreased fatigue, increased stress and increased sleep quality was associated with increased odds of having a migraine attack occur in the afternoon compared to having a morning onset attack. In Section D, each variable was modelled individually with phase as the primary independent variable to assess whether there were association with the specific migraine phases. Further pairwise comparisons were used to test for differences in each variable between each phase level. Fatigue which was important in sections A and B displayed migraine type mediated effects on fatigue across the prodrome and migraine phases. Age and employment mediated effects of phase on mood were observed, with older participants displaying poorer mood in the postdrome compared to the interictal phase and unemployed participants displaying poorer mood in the migraine phase compared to the interictal phase. No effects of diary sleep timing variables and phase were observed in the models. However, pairwise comparisons revealed Sleep Onset was marginally earlier in the Interictal, and Prodrome phases compared to the Migraine phase. As well as this, participants reported more sleep disturbances in the Migraine phase compared to the prodrome, although no differences in reported disturbance duration were observed. Although sleep onset was earlier in the interictal phase, interictal diary wake up time was also earlier compared to the migraine phase. An effect of phase was observed for Fitbit Sleep Inertia, with participants taking longer to get out of bed following wakeup in the postdrome compared to the interictal phase. Pairwise comparisons further observed greater inertia in the postdrome phase compared to the prodrome and migraine phases. As well as this, an effect of phase on nap duration was observed, with greater nap duration in the prodrome and postdrome phases compared to the interictal phase. Pairwise

comparisons of nap duration also observed greater nap duration in the prodrome, postdrome and interictal phases compared to the migraine phase.

Section E modelled the neuropsychological variables with session as the primary predictor. Pairwise comparisons were used to examine differences between session levels. No clear pattern in performance was observed across session levels with baseline performance being the poorest for many of the test variables. Limitations of repeated measure designs in neuropsychological testing is addressed alongside unaccounted for variance across sessions.

In Chapter Six, the interview data on participants' experience participating in the longitudinal study (outlined in Chapter Five) were analysed. Results from this chapter highlighted three themes regarding participation; *Reasons for Participating*, *The Burden of Participating*, and *Considerations for Future Research*.. Participants spoke of *Reasons for Participating* that were associated with furthering research into migraine and being able to use the study as an opportunity to reflect on one's migraine experience. *The Burden of Participating* included some difficulties associated with keeping up with participation over the study duration and discomfort continuously wearing the Fitbit tracker. The most informative and potentially harmful experience referred to the neuropsychological assessment which directly impacted participants by triggering pain and symptoms of nausea. Finally, the theme of *Considerations for Future Research* was less frequently observed in the data and included minor changes to study procedure. This chapter concludes that specific considerations should be taken when choosing neuropsychological assessments to prevent further harm and discomfort to participants.

7.3 Situating the Findings within the Theoretical Framework

The primary aim of this thesis was to investigate migraine as a cyclical neurological disorder with biological, psychological, behavioural, and social manifestations. The conceptual foundation of this research draws on multiple related but distinct bodies of literature, specifically research on biological rhythms and cyclical migraine phases known as the prodrome and postdrome defined by a number of psychological and behavioural symptoms (Bose et al., 2018; Karsan & Goadsby, 2018; Roenneberg et al., 2019; Takahashi et al., 2019). Regarding the circadian framework, the findings observed in Chapter Three observed some differences in sleep patterns between individuals with migraine and healthy controls. This study suggested that individuals with migraine slept longer on work days and as a weekly average, however no difference in phase of entrainment or circadian misalignment was observed. In Chapter Five, none of the sleep variables were associated with migraine occurrence. However, some differences were observed between phase level comparisons' with sleep onset in the Migraine headache phase being slightly later than the interictal and prodrome phases. However, this difference was marginal and may reflect difficulty falling asleep in the migraine headache phase, potentially due to symptoms associated with the headache such as pain, and nausea (Vgontzaz & Pavolic, 2018). It is also possible that coping mechanisms during the attack, such as lying down in a dark room, reduced the exposure to circadian time-givers specifically, light, meal times and activity (Roenneberg et al., 2003). However, this is beyond the scope of the findings presented in this thesis and warrants further investigation. The cross-sectional study described in Chapter Three further observed differences in self-regulation of eating and with associations of appetite changes in migraine onset observed in Chapter Five, suggesting the potential of dysregulated

appetite and meal timings. However, the circadian nature of these significant eating factors is speculative and beyond the scope of this research.

Findings regarding the presence of the hypothalamic-based behaviours in migraine were more promising. In Chapter Five, migraine onset was associated with fatigue, stress, appetite changes and changes in perceived body temperature, emphasising the role of hypothalamic based behaviours in migraine. This was also evident in Chapter Four, where participants spoke of cravings, feeling cold in the body and tiredness prior to a migraine headache. The role of phase in these associations is less clear, with the lagged analysis finding no significant effect of these factors at prodromal windows of 24-, 48- and 72-hours. However, the validity of this analysis is questioned through the use of a 'clean' migraine variable, which removed migraine attacks that did not have a 48-hour migraine free period before and after an attack. Although this thesis focused on the circadian and cyclical characteristics of migraine, Chapter Four emphasised the broader subjective lived experience of migraine, which went beyond the theoretical framework.

When considered together, all of the findings presented in this thesis convey migraine as implicating all aspects of individual functioning. Migraine has physiological components, of course, but it also impacts the individual psychologically, behaviourally and socially (Buse et al., 2018; 2019). The psychological impact of migraine can be observed in Chapter Two where numerous studies observed a global level of cognitive impairment and domain-specific cognitive impairment in individuals with migraine. Chapter Four further conveyed the psychological impact of migraine through participants' own subjective experiences of cognitive impairment, where many spoke of 'not being able to think properly' leading up to, and following a migraine. In Chapter Four, the

psychological impact went beyond cognition, as the first theme *mental wellbeing* discussed the affective impact of migraine and the shame, guilt and anxiety associated with living with the condition. Psychological factors were also evident in Chapter Five, as fatigue and stress were associated with migraine onset, and fatigue with migraine duration and severity. Behaviourally, in Chapter Three, differences in sleep and eating behaviours were observed in individuals with migraine compared to those without migraine. The behavioural impact was also observed within individuals with migraine. In Chapter Five, a number of behaviours such as sleep onset, sleep inertia and napping were implicated across the migraine phases. Migraine extended beyond the individual as the social impact of migraine was poignantly depicted throughout Chapter Four. Migraine invaded all aspects of the participants' daily lives including relationships with family, friends, the wider community and in turn, the participants' sense of self, further suggesting the biopsychosocial model may provide a useful theoretical framework for future research on migraine (Lehman et al., 2017).

7.4 Circadian, Sleep and Eating Factors in this Thesis

No significant effects of circadian sleep timing variables such as MSFsc and SJL were observed in the present research. Existing research on the circadian relationship of migraine has observed significant associations using the Morning-Eveningness Questionnaire which observed psychological circadian preference (Sullivan & Martin, 2016). The current study however used the Munich Chronotype Questionnaire which records actual sleep timing behaviours rather than preference. Existing research using the MCTQ further reports no significant differences or

associations (van Oosterhout et al., 2018). Furthermore, the MCTQ relies on self-report sleep timings and assumes a consistent sleep schedule on work and free days and may not reflect objective sleep timing measurements. Studies which use actigraphy measures of midsleep timing have found significant differences in MSFsc compared to non-migraine controls (Ong et al., 2018). The relationship between migraine and MSFsc has further been observed in individuals who report a consistent pattern to attack (Im et al., 2019). The preferential timing of migraines was not assessed in the cross-sectional study and as such could not be examined in relation to MSFsc. Furthermore, while time of attack onset was assessed in the longitudinal study, work and work-free days were not distinguished. The lack of circadian associations was further observed using the Sleep Regularity Questionnaire which found no difference in circadian rigidity or sleep continuity between individuals with migraine compared to non-migraine controls. It is possible that this may reflect strategies by individuals with migraine to avoid perceived triggers by maintaining a consistent sleep pattern (Sullivan et al., 2022). Another explanation may acknowledge that associations between migraine frequency and sleep continuity was nearly significant with a trend of greater mean sleep continuity in individuals with chronic, (more than 15 migraine days a month) migraine.

The circadian relationship on eating behaviours is less studied in the literature, albeit known that the timing and composition of meals impact circadian rhythm synchronisation between the peripheral and central clocks (BaHamman & Pirzada, 2023). Furthermore, the timing of meals influences sleep timings with early eating causing individuals to sleep and wake earlier (Blum et al., 2023). In the cross-sectional study, individuals with migraine displayed significantly lower levels of self-regulation of eating behaviours compared to individuals without migraine.

Interestingly, in section one of the longitudinal study (Chapter Five) model 10 having *unusually* increased or decreased appetite statistically affected migraine onset suggesting that changing one's typical eating behaviour was associated with migraine onset. This was similarly recalled by participants in the qualitative study in Chapter Four, who spoke of having specific cravings before they experience a migraine headache. This is in line with existing research which suggests appetite changes to be an early indicator of attack onset (Ashraf et al., 2025). Such symptoms may reflect early homeostatic dysfunction by which the relationship with circadian rhythms and circadian anatomy cannot be ignored (Eigenbrodt et al., 2022; Martins-Oliveira et al., 2021). However, the role of eating regulation including meal timing and circadian rhythms in migraine needs to be explored further. The role of homeostatic processes and potential of hypothalamic dysfunction in migraine may be strengthened by the finding of increased fatigue, having unusually increased or decreased appetite and feeling unusually warm or cold in Section A of Chapter Five. Interestingly, as well as having specific cravings, in Chapter Four, participants also spoke of “feeling cold in the body”, yawning and tiredness, mirroring the findings observed in Section A, Chapter Five. Minimal research exists on impaired thermoregulation in migraineurs however, research by Ordás et al. (2013) observed increased axillary temperature on migraine days compared to non-migraine days.

The findings on sleep in this research were not consistent with those in the literature which suggested an important role of sleep quality in migraine pathophysiology (Schumacher et al., 2023). Findings from the cross-sectional study indicated no difference in self-reported sleep quality between individuals with migraine versus individuals without migraine or between migraine frequency groups. However, mean sleep quality displayed a trend towards reduced sleep quality with

increasing migraine frequency albeit not significant. In the longitudinal study, no association between sleep timing variables, sleep quality or sleep efficiency were observed however migraine frequency was not examined (Schumacher et al., 2023).

Pairwise comparisons did reveal slight differences in sleep variables across phases. Diary Sleep Onset was later in the interictal phase compared to the prodrome and migraine phases, as well as this, participants woke up slightly later in the migraine phase. As sleep variables were not associated with migraine onset in section A, our findings are more consistent with a therapeutic and strategic role of sleep in the migraine phases (Rains et al., 2008). Sufficient sleep duration is often also perceived as a means to prevent an attack (Sullivan et al., 2022). This may further help to explain the findings in the cross-sectional study which observed significantly greater average weekly sleep duration and workday sleep duration in individuals with migraine compared to individuals without migraine. The therapeutic role of sleep in migraine may further be supported by the finding of longer nap duration in the prodrome and postdrome phases of an attack compared to the interictal phase. However, it may also represent hypothalamic dysregulation consistent with prodromal functioning (Goadsby et al., 2017; Karsan & Goadsby, 2020; Rains et al., 2008). Interestingly, nap duration in the migraine phase was shorter than interictal nap duration. In addition, we observed greater sleep disturbance frequency in the migraine phase compared to the prodrome phase. Taken together, it is possible that sleep may be hindered during the migraine phase as a result of pain and nonpainful symptoms associated with migraine such as nausea, cutaneous allodynia, photophobia and phonophobia (Sharp et al., 2024). We also observed an effect of phase on Fitbit Sleep Inertia with greater inertia being observed in the postdrome phase, following headache resolution compared to the prodrome,

migraine and interictal phases. Greater sleep inertia may be caused or associated with a number of factors including high sleep pressure due to sleep loss, circadian dysregulation and waking from slow wave sleep (Hilditch & McHill, 2019). The observed increased sleep inertia in the postdrome may be contextualised by findings which report increased slow-wave sleep during an attack with REM suppression to enable restoration following an attack however this needs to be explored further (Stanyer et al., 2021).

7.5 Implications

The present research has compellingly argued the dimensional nature of migraine, that goes beyond the pain of headache and the associated symptoms of nausea, phonophobia and photophobia. The impact of migraine can be observed physiologically, psychologically, behaviourally and socially (Buse et al., 2019; 2018; Richardson & Diaz, 2024). In the present research and existing literature, psychologically, migraine is associated with cognitive impairment and reduced mental wellbeing (Amiri et al., 2019; Richardson & Diaz, 2024). The participants in this Chapter Four described anxiety, and negative emotions of guilt and shame. Alongside the multidimensional impact of migraine, recognition that pain perception and chronic pain experiences are influenced by biological, psychological and social factors further supports the need for migraine care to expand beyond pharmacological treatments (Gatchel et al., 2007; Meints & Edwards, 2018). Psychological treatments in migraine such as cognitive behavioural therapy would help to reduce patients' maladaptive thoughts and beliefs about their migraine (Amatrudo et al., 2023; Bond et al., 2015). This would then help to alleviate the feelings of guilt and shame that were observed in this research (Chapter Four). Alongside this, cognitive behavioural therapy has been found to be effective in

reducing migraine frequency, pain severity, avoidance behaviours as well as pain-related cognitive impairment (Bae et al., 2021; Klan et al., 2022). This coupled with mindfulness-based interventions, which are also effective in relieving the impact of pain, could substantially improve the quality of life of migraine patients (Prohaska & Matthias 2023). The clinical utility of psychological treatments is evidenced in the adaptability of the treatments into online formats, which in turn enable greater accessibility for a large proportion of the population (Grazzi et al., 2026).

Designing and implementing online psychological interventions would enable greater quality of life in terms of psychological and physiological migraine outcomes irrespective of the level of disability such as that which is required to access specialist care (Bromberg et al, 2012; Hedborg & Carin, 2011; Huguet et al., 2024). Online learning materials could also be made available to educate family, friends and employers on the reality of migraine. This would work to help alleviate the social impact of migraine stigma, and its consequential physical and psychological impact (Buse et al., 2019; Shapiro et al., 2024; Young et al., 2013).

Online access to treatment is particularly relevant for the Irish context as there is a greater reliance on primary care in migraine management than other European countries due to a lack of specialist services (Darcy et al., 2023; Vaghi et al., 2023). While this is theoretically a suitable method of delivering care, there are limitations to the level of knowledge and range of treatments available to general practitioners in Ireland. While the European Headache Federation suggests that majority of migraineurs should be treated in a primary care setting, it also suggests a level of quality that is not regulated or enforced in Irish health services (Steiner et al., 2019). For example, the European Headache Federation suggests headache and migraine education should be provided by specialist centres to general practitioners

in the designated jurisdiction (Steiner et al., 2019). This should be enforced through mandatory training programmes to enable at least one trained practitioner per clinic, across the country to ensure a basic standard of treatment is met. This could then be expanded to include the ability to prescribe the newest migraine-specific medications such as Calcitonin Gene Related Peptide (CGRP) targeting therapies, which are highly regulated under the Health Service Executive's (2025) Medicines Management Programme's Managed Access Protocol. Although, the American Headache Society recommends CGRPs as a first line treatment option, the Managed Access Protocol ensures CGRPs are only available through prescription by approved headache specialists following ineffective trialling of a minimum of three conventional and more affordable migraine treatments including Triptans, Beta-Blockers and Flunarizine (Charles et al., 2024; Health Service Executive, 2025).

7.6 Limitations

There were various noteworthy limitations to the studies included in this thesis.

7.6.1. Scoping Review presented in Chapter Two.

The results included in the scoping review were very heterogenous in nature making it difficult to capture the neuropsychological profile for migraine. Furthermore, performance varied within tasks, with some studies reporting significant differences while others observed no significant differences. Similarly, little information on the impact of comorbid psychiatric disorders was included across the studies. The sporadic nature of migraine is a significant limiting factor to all research in migraine with no exception to cognition. Most of the studies included in the review were during the interictal phase or during the attack; and it is difficult

to exclude the potential of an attack occurring after participation; meaning the phase of functioning cannot truly be guaranteed.

7.6.2. Sampling

A general limitation of the research included in this thesis is the restriction placed on study duration which directly impacted the sample size and number of observations across all of the studies. As a result, the sample sizes in each study were small. All of the research studies included in this thesis availed of non-random convenience sampling. Alongside this, the sample of participants in the cross-sectional chapter were made up of predominantly female participants and entirely for the longitudinal and qualitative chapters. As such the findings from this thesis may not be generalisable to the general population particularly male migraineurs.

Recruitment for the empirical chapters of this thesis was in conjunction with the Migraine Association Ireland and as such may represent a subset of individuals with migraine that is particularly severe, which in turn caused the participants to reach out to the association for support and information. Finally, as the research was not conducted alongside a migraine clinic, it is possible that the control group of non-migraine individuals may include participants who have undiagnosed migraine or vice versa whereby individuals with migraine have been incorrectly and potentially self-diagnosed. All of the research in this thesis relied on self-reported diagnosis of primary migraine by a licensed medical practitioner.

7.6.3. Qualitative Study presented in Chapter Four

The semi-structured interviews were conducted by a novice researcher, with no previous experience in qualitative data collection. Furthermore, there were times during the interview which may have benefited from a more experienced researcher

to probe individuals to elaborate their answers to a greater degree. The primary researcher was further diagnosed with migraine and the individual bias in shaping the interview schedule and identifying themes in the data is possible. Personal experience was evident during the interview process at times through moments aimed to highlight understanding of the participants through shared experiences.

7.6.4. Longitudinal Study presented in Chapter Five

An important limitation of the sleep diary used in the longitudinal study was the lack of standardised measures. For example, the scale used to measure pain severity used the terms not at all (1) and extremely (10) to describe pain severity. More conventional scales would avail of a scale which categorically defines pain as mild, moderate and severe. Furthermore, the use of headache and migraine-specific measures such as the HIT-6 to assess headache impact would have enabled more informative results that could be compared more directly to existing literature on migraine. This is a major limitation of the study. Furthermore, confounding factors such as medication use were not addressed in the current research. It is also likely that daily measurement was not sufficient to capture phase-related changes in behaviour. A recent finding by Schwedt et al. (2025) found that prodrome symptoms were followed by migraine within 1-6 hours in 81.5% of cases. This percentage significantly reduced to 4.5% between 6 and 24 hours. Another limitation of this chapter includes the analyses described in Sections B and C which use a modified migraine onset variable that ensured no overlap between prodrome and postdrome phases. While this enabled examining specific phases, it does not reflect the true migraine experience where a migraine may occur a few hours after or a day after an attack has ended.

7.6.5. Neuropsychological Assessment

Due to the nature of migraine as being sporadic and unpredictable, it was decided that it would be better to conduct remote neuropsychological assessments. While there are benefits such as making it easier for participants to complete by eliminating the scheduling and travel factor associated with lab-based experiments; there are multiple limitations such as a lack of control across and within individual assessments. For example, the environment that the participant is in may have fluctuated across tests; noise levels, disruptions and technical difficulties. Alongside this, it was difficult to ensure participants were adhering to the study procedure that was asked when completing the tasks. Efforts to limit the effect of practice across testing sessions added a level of variance to the difficulty across tasks. For example, each rendition of the Trail Making Tests included new trail patterns and different coloured stimuli were used in the Go/No-Go tests. As a result, some trails in the TMT may have had sequences which were relatively close together, making it easier to identify the following number or letter needed to connect the trail. In the same regard, some Go/No-Go may have been easier or harder with certain colour pairings having predetermined meanings such as red being used as a no-go stimulus and green being used a go stimulus; or vice versa. The study design further required participants to complete neuropsychological assessments within 24 hours and 48 hours following the cessation of migraine pain. However, research by Giffin et al. (2016) found that for the majority of participants, the postdrome phase lasted no longer than 6 hours and very rarely more than 24 hours. As such, the temporal layout of the present study may not have captured the greatest impact on cognitive

performance. Furthermore, it was not possible for the participants to ensure that the neuropsychological assessment was completed in the prodrome phase as there were occasions where migraine attacks overlapped in such a way that it theoretically would have been simultaneously both the postdrome and prodrome phases.

7.7 Strengths

There were a number of strengths with the research presented in this thesis. The scoping review was one of the first to try to characterise the neuropsychological profile of migraine, moving a step closer to understanding the cognitive facet of migraine. Alongside this, the scoping review highlighted key limitations to the existing research which need to be resolved moving forward.

The longitudinal study was successful in terms of sample retention and design which enabled 1,235 days of data to be recorded of which included a total of 303 migraine days. The data is comprehensive with a number of self-report and actigraphy variables. In many ways, the longitudinal study is accessible as it used non-medical grade objective measures of sleep via Fitbits rather than polysomnography which requires significant financial resources and is particularly burdensome on participants. Alongside this, the study used remote neuropsychological assessment which is also more cost effective and enables assessment in otherwise hard to research populations. The present study offers a research prototype that has shown to be effective in researching sporadic disorders such as migraine as emphasised by the number of migraine days recorded and general sample retention rates. Not only is the approach effective but avails of a range of methodologies which offers a novel insight into migraine. Not only does the thesis include cross-sectional, longitudinal, objective and subjective insights but also

a range of analytical approaches including quantitative (frequentist and Bayesian paradigms) and qualitative. This is a major strength of the thesis as it enables a multifaceted insight into the holistic experience of migraine.

7.8 Present Findings and Future directions

The present research aimed to examine the role of biological rhythms in migraine alongside investigating functioning across the migraine cycle. The research in this thesis was unable to identify circadian factors in migraine and this remains an important question to be asked in future studies. The longitudinal study described in Chapter Five did not distinguish between work days and free days to enable an examination of the role of chronotype in migraine onset, within individuals. Future research using similar designs, should include this as a daily measurement alongside other external determinants of individual sleep timing. The concept of distinct phases prior to and following the migraine headache also needs to be examined further as this research did not observe many-phase specific associations with self-report sleep timing, duration and quality or Fitbit actigraphy. One major methodological limitation with examining phase specific functioning arises from the distinction between phases; at which point does a phase begin and end, indicating the start of the new phase? This is particularly difficult when many individuals with migraine experience concurrent prodrome and postdrome in subsequent migraine attacks. To counteract this, our analysis used a modified “clean” migraine variable, which removed attacks that occurred within 48-hours of another attack. However, very few findings were observed and nothing that sheds light on the role of the hypothalamus in these phases. We argue that while this enabled examining isolated

phase functioning, it is not representative of migraine. This remains a difficulty for migraine research, and perhaps in considering the typical length of these phases the number of migraine events excluded could be reduced and more accurately reflect migraine. For example, research by suggests that the prodrome is observed 6 hours prior to migraine in the majority of cases (Schwedt et al., 2025). Further research is needed to replicate this, and determine the typical length of the prodrome but also the postdrome phase. If phase lengths are less than a day, multiple measurements would need to be done each day to capture changes in functioning and the increased burden of this must be considered.

In terms of cognitive impairment, there are a number of factors which implicate the neuropsychological profile of migraine. The continuous exposure to pain, particularly in chronic cases, increases the probability of general cognitive decline in individuals with migraine. Investigating cyclic cognitive impairment is further hindered by the need for repeated measure designs and remote assessment. A lot more research is needed to create remote assessment procedures and design measures which are sensitive to detecting this impairment but also that will remain unaffected by practice.

7.8.1 Study Specific Directions

Findings from the scoping review indicated the need for clear agreed upon consensus for conducting neuropsychological assessments in individuals with migraine. Guidelines are needed for what neuropsychological assessments should be used with consideration for repeated testing requirements. Future research on neuropsychological functioning in migraine must continue to investigate functioning across migraine phases and comparison of each phase with non-migraine subjects as

a means to assess the level of impairment. Further research must also account for the effects of medication and comorbid conditions such as mood and anxiety disorders which have been shown to implicate cognitive performance (Vuralli et al., 2018).

Further investigation into the role of circadian rhythms in migraine is needed as genetic research has highlighted a significant number of circadian genes implicated in the disorder (Benki et al., 2023). Furthermore, as sleep timing has not been shown to be associated with migraine in the current research, perhaps investigation into internal measures of melatonin and cortisol in relation to light sensitivity in the population may be more insightful. Alongside this, further investigation into eating behaviours and meal timings in migraine is needed to replicate, clarify and expand on the findings observed in Chapter Three. Furthermore, phase-specific changes in sleep suggest that sleep is more unstructured in the interictal phase (later sleep onset and awakening) with more disturbances. Future research is needed to determine if there are phase-specific sleep profiles.

Finally, the qualitative study highlighted that more work is needed on educating the wider population about migraine, as it is still misunderstood as *just a headache*. In the same regard, migraine care needs to expand beyond pharmacological treatments to include psychological approaches such as cognitive behavioural therapy, that address the difficulties associated with the condition not limited to anxiety, depression, guilt, shame. While the

7.9 Final Thoughts

The research presented in this thesis highlights the nature of migraine as a neurological disorder, the impact of which, goes beyond the characteristic of pain. In this thesis, individuals with migraine displayed behavioural differences in sleep and

eating behaviours compared to individuals without migraine. Alongside this, the phase analysis conducted in Chapter Five section three highlights the changes in self-reported and actigraphy measured behavioural variables across the migraine phases. The scoping review highlighted that a number of cognitive domains were impaired in individuals with migraine compared to those without migraine. However, the portrayal of migraine as a disorder beyond pain was elicited by the participants who took part in the semi-structured interviews outlined in Chapter Four. Migraine as a disorder impacts the individual physically, psychologically, and socially. The impact of migraine goes beyond the level of pain measured by a scale and urges the need of continued research into the non-painful effects of the disorder.

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Appendix A: Measures used in Chapter Three

A.1. The Munich Chronotype Questionnaire (Roenneberg et al., 2003).

Munich ChronoType Questionnaire (MCTQ)

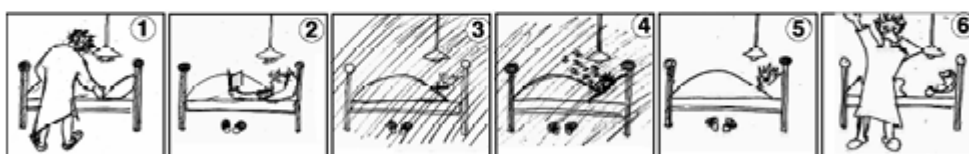
In this questionnaire, you report on your typical sleep behaviour over the past 4 weeks. We ask about work days and work-free days separately. Please respond to the questions according to your perception of a standard week that includes your usual work days and work-free days.

I have a regular work schedule (this includes being, for example, a housewife or househusband):

Yes ☐ I work on 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ days per week.

No ☐

Is your answer "Yes, on 7 days" or "No", please consider if your sleep times may nonetheless differ between regular 'workdays' and 'weekend days' and fill out the MCTQ in this respect.



Please use 24-hour time scale (e.g. 23:00 instead of 11:00 pm)!

Workdays

Image 1: I go to bed at _____ o'clock.

Image 2: Note that some people stay awake for some time when in bed!

Image 3: I actually get ready to fall asleep at _____ o'clock.

Image 4: I need _____ minutes to fall asleep.

Image 5: I wake up at _____ o'clock.

Image 6: After _____ minutes I get up.

I use an alarm clock on workdays: Yes ☐ No ☐

If "Yes": I regularly wake up BEFORE the alarm rings: Yes ☐ No ☐

Free Days

Image 1: I go to bed at _____ o'clock.

Image 2: Note that some people stay awake for some time when in bed!

Image 3: I actually get ready to fall asleep at _____ o'clock.

Image 4: I need _____ minutes to fall asleep.

Image 5: I wake up at _____ o'clock.

Image 6: After _____ minutes I get up.

My wake-up time (Image 5) is due to the use of an alarm clock: Yes ☐ No ☐

There are particular reasons why I cannot freely choose my sleep times on free days:

Yes ☐ If "Yes": Child(ren)/pet(s) ☐ Hobbies ☐ Others ☐, for example: _____

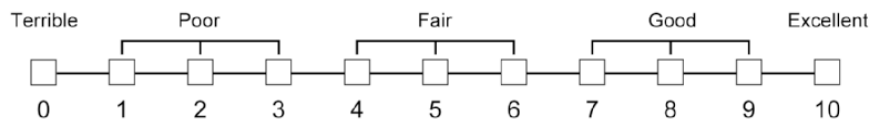
No ☐

A.2. Single-Item Sleep Quality Scale (Snyder et al., 2018).

INSTRUCTIONS:

- The following question refers to your overall sleep quality for the **majority** of nights in the **past 7 days ONLY**.
- Please think about the quality of your sleep **overall**, such as how many hours of sleep you got, how easily you fell asleep, how often you woke up during the night (except to go to the bathroom), how often you woke up earlier than you had to in the morning, and how refreshing your sleep was.

1. During the **past 7 days**, how would you rate your sleep quality overall?
(Please mark only **1** box)



A.3. The Sleep Regularity Questionnaire (Dzierzewski et al., 2021).

INSTRUCTIONS: Thinking of how you usually sleep, how much do you agree with the statements below. There are no right or wrong answers. Don't spend too much time on any one statement.

	NOT AT ALL	A LITTLE BIT	SOMEWHAT	MODERATELY	VERY MUCH
1. I go to bed at about the same time every night.....	☐	☐	☐	☐	☐
2. It takes me about the same amount of time to fall asleep each night.....	☐	☐	☐	☐	☐
3. I wake up for about the same number of times each night.....	☐	☐	☐	☐	☐
4. I spend about the same amount of time awake each night.....	☐	☐	☐	☐	☐
5. I wake up at about the same time each morning.....	☐	☐	☐	☐	☐
6. I get out of bed at about the same time each morning.....	☐	☐	☐	☐	☐
7. I feel about equally refreshed upon waking up each morning.....	☐	☐	☐	☐	☐
8. I am asleep for about the same amount of time every night.....	☐	☐	☐	☐	☐
9. I take (or do not take) a similar number and duration of naps each day	☐	☐	☐	☐	☐
10. My sleep on weekdays and weekends is about the same.....	☐	☐	☐	☐	☐

FACTOR LOADINGS:

Circadian Regularity Factor: Questions 1, 5, 6, 8

Sleep Continuity Factor: 3, 4

REMOVED ITEMS (DID NOT LOAD ON A FACTOR):

2, 7, 9, 10

A.4. The Adult Eating Behaviour Questionnaire (Hunot et al., 2016).

Adult Eating Behaviour Questionnaire

Please read each statement and tick the box most appropriate to you

	Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
I love food	☐	☐	☐	☐	☐
I often decide that I don't like a food, before tasting it	☐	☐	☐	☐	☐
I enjoy eating	☐	☐	☐	☐	☐
I look forward to mealtimes	☐	☐	☐	☐	☐
I eat more when I'm annoyed	☐	☐	☐	☐	☐
I often notice my stomach rumbling	☐	☐	☐	☐	☐
I refuse new foods at first	☐	☐	☐	☐	☐
I eat more when I'm worried	☐	☐	☐	☐	☐
If I miss a meal I get irritable	☐	☐	☐	☐	☐
I eat more when I'm upset	☐	☐	☐	☐	☐
I often leave food on my plate at the end of a meal	☐	☐	☐	☐	☐
I enjoy tasting new foods	☐	☐	☐	☐	☐
I often feel hungry when I am with someone who is eating	☐	☐	☐	☐	☐
I often finish my meals quickly	☐	☐	☐	☐	☐
I eat less when I'm worried	☐	☐	☐	☐	☐
I eat more when I'm anxious	☐	☐	☐	☐	☐
Given the choice, I would eat most of the time	☐	☐	☐	☐	☐

	Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
I eat less when I'm angry	☐	☐	☐	☐	☐
I am interested in tasting new food I haven't tasted before	☐	☐	☐	☐	☐
I eat less when I'm upset	☐	☐	☐	☐	☐
I eat more when I'm angry	☐	☐	☐	☐	☐
I am always thinking about food	☐	☐	☐	☐	☐
I often get full before my meal is finished	☐	☐	☐	☐	☐
I enjoy a wide variety of foods	☐	☐	☐	☐	☐
I am often last at finishing a meal	☐	☐	☐	☐	☐
I eat more and more slowly during the course of a meal	☐	☐	☐	☐	☐
I eat less when I'm annoyed	☐	☐	☐	☐	☐
I often feel so hungry that I have to eat something right away	☐	☐	☐	☐	☐
I eat slowly	☐	☐	☐	☐	☐
I cannot eat a meal if I have had a snack just before	☐	☐	☐	☐	☐
I get full up easily	☐	☐	☐	☐	☐
I often feel hungry	☐	☐	☐	☐	☐
When I see or smell food that I like, it makes me want to eat	☐	☐	☐	☐	☐
If my meals are delayed I get light-headed	☐	☐	☐	☐	☐
I eat less when I'm anxious	☐	☐	☐	☐	☐

Adult Eating Behaviour Questionnaire - Scoring information

		Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
EF	I love food	☐	☐	☐	☐	☐
FF	I often decide that I don't like a food, before tasting it	☐	☐	☐	☐	☐
EF	I enjoy eating	☐	☐	☐	☐	☐
EF	I look forward to mealtimes	☐	☐	☐	☐	☐
EOE	I eat more when I'm annoyed	☐	☐	☐	☐	☐
H	I often notice my stomach rumbling	☐	☐	☐	☐	☐
FF	I refuse new foods at first	☐	☐	☐	☐	☐
EOE	I eat more when I'm worried	☐	☐	☐	☐	☐
H	If I miss a meal I get irritable	☐	☐	☐	☐	☐
EOE	I eat more when I'm upset	☐	☐	☐	☐	☐
SR	I often leave food on my plate at the end of a meal	☐	☐	☐	☐	☐
FF*	I enjoy tasting new foods	☐	☐	☐	☐	☐
FR	I often feel hungry when I am with someone who is eating	☐	☐	☐	☐	☐
SE*	I often finish my meals quickly	☐	☐	☐	☐	☐
EUE	I eat less when I'm worried	☐	☐	☐	☐	☐
EOE	I eat more when I'm anxious	☐	☐	☐	☐	☐
FR	Given the choice, I would eat most of the time	☐	☐	☐	☐	☐
EUE	I eat less when I'm angry	☐	☐	☐	☐	☐
FF*	I am interested in tasting new food I haven't tasted before	☐	☐	☐	☐	☐
EUE	I eat less when I'm upset	☐	☐	☐	☐	☐
EOE	I eat more when I'm angry	☐	☐	☐	☐	☐
FR	I am always thinking about food	☐	☐	☐	☐	☐
SR	I often get full before my meal is finished	☐	☐	☐	☐	☐
FF*	I enjoy a wide variety of foods	☐	☐	☐	☐	☐
SE	I am often last at finishing a meal	☐	☐	☐	☐	☐
SE	I eat more and more slowly during the course of a meal	☐	☐	☐	☐	☐

		Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
EUE	I eat less when I'm annoyed	☐	☐	☐	☐	☐
H	I often feel so hungry that I have to eat something right away	☐	☐	☐	☐	☐
SE	I eat slowly	☐	☐	☐	☐	☐
SR	I cannot eat a meal if I have had a snack just before	☐	☐	☐	☐	☐
SR	I get full up easily	☐	☐	☐	☐	☐
H	I often feel hungry	☐	☐	☐	☐	☐
FR	When I see or smell food that I like, it makes me want to eat	☐	☐	☐	☐	☐
H	If my meals are delayed I get light-headed	☐	☐	☐	☐	☐
EUE	I eat less when I'm anxious	☐	☐	☐	☐	☐

* Reversed items

Enjoyment of food	=	item mean EF
Emotional over-eating	=	item mean EOE
Emotional under-eating	=	item mean EUE
Food fussiness	=	item mean FF
Food responsiveness	=	item mean FR
Slowness in eating	=	item mean SE
Hunger	=	item mean H
Satiety responsiveness	=	item mean SR

Strongly disagree =1, Disagree = 2, Neither agree nor disagree = 3, Agree =4, Strongly agree =5

Appendix B: Additional examples of themes and subthemes.

Theme 1: Mental Wellbeing (N=9)

Subtheme 1: Fear of migraine (N = 7)

Participants expressed persistent avoidance of social events because of past experiences, which meant they had to cancel plans with friends. Some participants expressed that it was easier not to make plans because of the likelihood of having a migraine and not being able to follow through. As much as avoidance was a mechanism to protect the individuals from ‘triggering’ an attack, it also worked to prevent feelings of disappointment and guilt.

“If I don't have plans, then I don't have to cancel them. And then I don't get, you know, I won't be getting as upset.” Participant 8)

“I'd be anxious about making plans of friends because I used to know I'd have to cancel most of the time.” (Participant 5)

At times, avoidance was partially based on presumption and associations derived from similarity rather than experience explicitly. For example, Participant 10 mentioned they would not attend a concert because of numerous factors relating to overstimulation; however, it was presumed that this would likely apply to similar situations such as being in a crowd:

I find it hard to let go and have a really great time. I know if I do that, I'll get a migraine. So, I'm stopping myself going to a concert, for example. That would be an absolute no-no. Or going to a big, crowded place, even if it's not a concert, because that would be, probably a no-no. (Participant 10)

A level of avoidance was also expressed in relation to employment, where the individual has some autonomy around their career and its progression. One participant who expressed being particularly career-oriented, spoke of limiting

themselves by not accepting career progression opportunities due to the appraisal of these opportunities as being potentially stressful or not knowing how their migraines would be affected by the change.

It's definitely held me back and I don't think I would have liked to have thought of that years ago, but now I can see definitely it held me back from putting myself forward for things.

...

I know I'm probably capable of more and more interesting work, but for me, the fact that there's no travel, it's not a particularly stressful job. That's really important to me, and I know there's probably other things I'd love to do. But I know I hold back 'cause. I'm going, but if I do that now, that's going to be a big change. I'm going to have to learn a lot. It's going to be a different environment, learning things in a new team. Oh God, it's going to be really stressful. Is that going to kick off my migraine and make it worse when I'm so much better than I used to be? (Participant 9)

Subtheme 2: Self-conscious emotions

Lack of understanding seemed to act as a mediating factor for experiences of guilt.

At times, migraineurs felt their experiences to be valid reasons for not being able to live up to social norms and expectations. However, some participants felt others were not as accepting or understanding, as though the participants were making excuses for their behaviour or that it was generally unjustifiable.

I felt that they might not understand the realities of it, and I felt like every time I told them I couldn't go because I had a migraine. I felt like I was nearly giving an excuse, and it was a cop out.

...

It was just lack of understanding. So, I suppose it probably did contribute to the kind of uneasiness I felt with bowing out of social things. (Participant 5)

Interestingly but not surprisingly values and understandings were influenced by culture as demonstrated by one participant who emphasised the perception of migraine in comparison to other illnesses and disabilities: *“I struggle with the guilt of explaining it to people because I know there’s... maybe this is a very Irish thing, or not just a human thing, there’s so much worse that it could be and there is, and I’m very grateful for that. (Participant 10)*

Ultimately, guilt was a result of not living up to social expectations or individual and group values. However, there was a conflict in belief by the participants who themselves expressed guilt shaped by the external environment of society and a sense of justification based on their own lived experience with migraine as a barrier: *“It’s the migraine that I need people to understand it and not to make me feel guilty because I don’t want to be going through this, I don’t want to be experiencing it” (Participant 8)*

For two participants, their migraine and experiences of guilt had become so severe that they began to impact their sense of identity and perception of themselves. As a result, these participants expressed shame in who they had become and the lack of agency they felt on a daily basis. For example, *participant 1* expressed a sense of identity related to driving, stating that they are the driver of the family, they loved to drive and the freedom that came with it. However, following the worsening of their migraine, their ability to drive was impacted. The participant recalled:

I was literally physically falling down and couldn’t move from that spot and couldn’t see and couldn’t move. And I was like, I can’t... I can’t do this.

I can't let this be my life. And now, like the driving at night, I had to give in to that. That really, really got me down. I was like "I'm, I'm 45. I'm not 75" you know. (Participant 1)

This segment really highlighted the impact on the participants identity and a level of shame as they reflect on the limitations they have to accept as a result of migraine. Similarly for participant 10, migraine had interfered with their career and resulted in having to retire. This participant spoke of the difficulty associated with not having their career that they worked so hard for, stating:

It has impacted completely my ability to work, and I find that really impacts my well-being. That impacts my ability to feel like I have a contribution to feel you know to the world and that I'm making a contribution to the house financially
...
It impacts... how I feel other people see me and how I see myself. So that impacts, my well-being... always in the background. (Participant 10)

Subtheme 3: Acceptance and Resilience (N = 7)

The refusal of defeat was emphasised as they discussed the dread associated with pregnancy and parenting. *Participant 5* discussed thinking about their future in starting a family which would be made difficult due to the restrictions around medication during pregnancy and breastfeeding along with the thought of having to be present and able for an infant regardless of the pain associated with migraine. However, as much as the thought of starting a family under these conditions was particularly troublesome, the participant surely expressed

“I’m going to be having a family as long as I can, no matter what, anyway. And I’ll just deal with the next thing when it comes to it. But it’s definitely not ideal to have all those worries in the back of your mind.” (Participant 5)

This dichotomy of resistance and acceptance was further highlighted by Participant 1 in the statement:

“I don’t want it to beat me, and I feel that I could. I could easily just hideaway in bed now. Sometimes I do. Don’t get me wrong. Sometimes I’m like, no, I can’t handle this, and I just need to go to bed.” (Participant 1)

However, the importance of not allowing the fear of a migraine occurring was also emphasised

I believe that it’s... it can be psychological. Like, I do believe that if you let it in there and decide, OK, these migraines have taken me over, if you let that happen, you will. You will fail as a you will end up being debilitated. You will end up staying at home.” It was emphasised by Participant 5 who stated with reference to their migraine diagnosis: *“It’s not going to go away. So, you just have to learn to live with it in some way. (Participant 1)*

Theme 2: Treatment: Trial and error

Subtheme 1: Can’t rely on medication (N = 9)

The reliance on acute medication to treat migraine was limited by the strict nature of migraine-specific medications, where often there is a very limited recommended dosage per month due to the high risk of overdose. As a result, participants spoke of having to ration their medication, trying to weigh the positives and negatives

associated with taking the medication for each attack. In particular, participants spoke of the difficulty associated with trying to decide whether to take medication due to the fear of needing it for a future attack, which may be worse.

But there is that always at the back of your head. Will I take something? Will I not? because then you're thinking "OK, well, if I take something today and in two days' time I get a worse headache, I can't take anything because I've taken it already", you know? And you can only take so many days. So, there is that constant will I, won't I, you know. And people say, why didn't you take something? So, I'm saving it for when it's really bad, when it's really bad, you know. (Participant 7).

However, even when participants decided to take medication, there was a lack of reliability on whether the medication would work to relieve the pain or prevent the attack from progressing. This was expressed more implicitly through passing statements such as from Participant 10 who said:

"Many of those migraines would either not go away, so the medication wouldn't work, or the medication would work but it comes back after six hours because I'm still working" (Participant 10).

Medication, for many, was not a definite solution to relieving an attack:

"The reality would have been kinda taking painkillers and going to going to bed for the day and trying to get over it. Do you know what I mean?" (Participant 8).

Migraine is complicated further by the potential worsening of the condition to be chronic with more frequent attacks that become less responsive to medication over time, alongside the increased potential of developing medication-overuse headache.

As time went on, they've gradually got more and more frequent and more difficult to treat and the, the acute attack became more difficult to treat and they got worse, I would say about, about 2004, 2005, so probably when I was thirty, they started getting really problematic. So, really frequent. I started getting... Less... again, less (of a) response to the acute medication.

(Participant 10)

This situation was complicated further in individuals who had secondary pain conditions. *Participant 10*, spoke of trying to manage two pain conditions where they are particularly conscious of keeping the medication to treat their migraine:

I have a lot of back pain issues, and you know it overlaps as in I'd like to take painkillers, and I should be taking different meds for back pain and sciatica, but I can't because that's going to give me... that's taking away one of the times I can take medications for my migraine. So, a lot of the time with my other pain, I don't take medication for it or very, very minimal... to maybe a topical gel or something that has little effect. And I don't take oral medication or injectable medication because I'm taking away one of the times that I can take it for the migraine, which is more significant. (Participant 10)

Theme 3: Fight for control (N= 10)

Subtheme 1: Try to control: I have to keep going (N= 10)

The unsustainable nature of coping with migraine in this way was highlighted by participants who expressed that it was to their detriment that the consequences of pushing themselves were felt. For example, *Participant 3* mentioned that while their work and social life aren't impacted, their migraines respond poorly to this approach, lasting for a couple of days at a time.

I don't generally miss out on anything with the migraine, I just kind of continue doing... which, I know is terrible and that's probably why they last so long, but... I probably just kind of continue on and feel like I want to die at the same time. (Participant 3).

This understanding of delayed recovery due to overextending oneself during and just after an attack was also mentioned by participant 9, who reflected on a day recent to the interview where they decided to take sick leave for a migraine attack and noticed the difference in their ability to recover when given the space and time:

I think other times I would have gone "I'll take my medication, and I'll go to work and I'll just push through, and I'll see how I am". Whereas that morning I just went, "no, don't do that, just stay in bed and sleep" and it was the right thing to do because I did recover a lot quicker, you know?

(Participant 9)

This worsening of the attack was also mentioned by participant 8 who spoke of their attacks becoming more chronic and unresponsive as they pushed forward with day-to-day tasks, not giving themselves the time they needed to recover: *"I was trying to keep going and trying to keep going and the attacks were becoming more frequent and were going on for longer."*

The need to be prepared for an attack was subjectively influenced by the perception of the likelihood of an attack occurring. For example, Participant 8 mentioned:

"I'd be a lot more alert if I couldn't sleep to have, just have everything, have my medication and things ready. Do you know what I mean? That the likelihood is it's coming on." (Participant 8)

A pre-emptive approach was not only mentioned with regard to making sure that the participants had medication at hand but also was mentioned with regard to planning events. For example, participant 5 discussed the stress of planning their wedding, an event which they perceived to be extremely triggering. For this participant, the reality of migraine was considered at every stage of the planning process to try to combat an attack occurring or to enable coping during the event should an attack occur.

“So much of the plans for the wedding and everything have, like, migraine has always been in my head during it and all the decisions... like, what I would be able for, what I know would not be good for me.” (Participant 5)

Subtheme 2: Loss of Control (N = 10)

At times, participants discussed how migraine had shaped their career choices by trying to find something they could fit into their lives with migraine.

Because I worked in the paramedics for one year and like, you just, you can't have migraines in that job because you can't just... you know, it's not as easy to just call in sick or leave work or whatever. And like, I remember having really like... coming down with migraines in the middle of a shift and you just, you just can't. So, that was part of... also, the, you know, the night shifts and the sleep routine and everything being all over the place that so that was part of my reasons as well for, for leaving that. (Participant 4).

The loss of control was often deeply felt by participants as mourning for the time lost to migraine or the life they could have had.

“It’s just like, just a general feeling of you’ve missed out on a day of your life, literally”. (Participant 4)

“It makes me feel down when I have to miss things or when I when it’s something that I’m looking forward to.” (Participant 5)

I’m after spending half the day in bed. That’s some of my weekend gone. And you know, I’m kind of a little bit beating myself up going, oh, you’ve wasted that time.

...

Yeah, it’s kind of it’s upsetting to kind of think... Yeah, I’m not living a life that I should be able to live (Participant 9)

“The loss of work and the impact it has on me socially and psychologically is definitely, probably the... that’s as big of a thing as the pain and the physical symptoms for me.” (Participant 10)

Theme four: It’s not just a headache (N = 10)

Subtheme One: The prodrome and postdrome (N = 10)

“Even sometimes the fatigue around an attack, either before it or afterwards, you’re just wiped out and just going “I’m too tired to do things” and that’s... just tasks, just seem so daunting.” (Participant 9)

Subtheme Two: Social Perception (N= 9)

The lack of understanding that the participants experienced was seen as dismissive to their migraine experience and made participating in society difficult as it enabled stigma and judgment from others.

“There are some people who are judging you, and they’re not important people in your life, but it’s still hard for it not to get on top of you.

So, they're judging why you're not working or why you're not out doing whatever it is that they think people should be doing.” (Participant 10)

At times, the difficulty in living with an individual with migraine was projected by the participants themselves:

“It's like... I know there's an awful lot of days in the month that are bad and my, and my husband feels the pressure of it, and I feel the pressure of it looking at him” (Participant 6)

It can be very tough on partners when you're constantly going “I don't, I don't want to go to the cinema, I don't feel like it. I don't want to eat the dinner you've cooked me, thank you; because I feel sick. I don't want to do XYZ. You know. It's hard on a partner to have to put up with that all the time. (Participant 10)

Appendix C: Study Information Sheet used in Chapters Four, Chapter Five and Chapter Six.

Study Information

Please read the following information carefully to make an informed choice about participating in this study.

Title of Study:

A cognitive-behavioural approach to Migraine as a cyclical disorder.

Purpose of Study:

I am a doctoral student in the Department of Psychology, Maynooth University. As part of the requirements for my PhD, I am undertaking a research study under the supervision of Dr Unai Diaz-Orueta and Professor Andrew Coogan.

Until recent years Migraine has commonly been perceived as just another headache. Migraine is a neurological disorder that causes severe headaches and physical and mental symptoms that can last for up to 6 days. These symptoms can include changes in how you feel and how your body and mind function.

Until recently researchers have ignored these nonpainful migraine symptoms which can impair wellbeing. It is hoped through this study we will learn more about nonpainful migraine experiences to provide better prediction and treatment of migraine.

This study has three goals:

- To see if there are any changes in the body or behaviour that happen before a migraine starts, and if these changes can be used to predict when a migraine will happen.
- To measure how people's thinking and mental processes are affected after a migraine attack has ended, during a period called the "postdrome phase."
- To raise awareness among researchers and medical professionals about the complexity of migraines and the need for more research into this condition.

Who Can Take Part:

Adults over the age of 18 years living in Ireland that have been diagnosed with primary migraine (not caused by another health difficulty) by a licenced medical practitioner. Need to have access to a mobile phone daily.

PLEASE NOTE: Due to the nature of the study individuals who with coexisting secondary physiological conditions which could be causing their migraine including but not limited to respiratory illnesses such as asthma and sleep apnoea cannot participate in this study. Similarly, individuals who are or have ever received treatment for psychiatric conditions are also excluded from participating in this

study. Individuals who are allergic to silicone are further excluded due to materials present in the active watches.

Do you have to take part?

No, you are under no obligation to take part in this research. It is entirely up to you to decide whether or not you would like to take part. If you decide to do so, you will be asked to sign a consent form and given a copy and the information sheet for your own records. If you decide to take part, you are still free to withdraw at any time without giving a reason and/or to withdraw your information up until data is irreversibly anonymised and compiled for analysis. A decision to withdraw at any time, or a decision not to take part, will not affect your relationships with Maynooth University or Migraine Association of Ireland.

Study Procedures:

This study will take measurements using Fitbit trackers, neuropsychological tests and daily migraine and sleep diary. The Fitbit trackers will take measures of heart rate, activity (distance, calories burned) and sleep measures including time of sleep onset, time of sleep offset, sleep efficiency and total sleep count. Heart rate variability may also be computed from heart rate data. The neuropsychological tests will measure mental processes such as attention and memory.

Study Instructions:

At the beginning of the study, you will complete the online neuropsychological assessment once. This will take approximately 20 minutes to complete.

The study will last for a duration of three months to try capture functioning leading up to and after migraine. For the duration of the study (90 days), it is required that:

- You wear the Fitbit on the wrist of your non-dominant hand every day and night, *except where the watch may be submerged in water or needs to be recharged.*
- You sync the Fitbit to the Fitbit application on your mobile phone and synchronise your devices daily using Bluetooth.
- You complete a paper booklet diary that includes brief questions to track your migraines and sleep

Important: You do not have to complete the diary and questionnaires if you are experiencing pain as a result of migraine. When you are no longer in pain, please continue to complete the daily questionnaire and mark in “yes” for the days you were experiencing migraine pain.

- If you have experienced a migraine, please click on the link sent to your email address provided. You will be redirected to an online platform

which will include some cognitive tests that will take 20 minutes to complete. You will be asked to complete the test again following a period of 2 days. Repeat this for up to three migraine attacks (six times).

- Please use the addressed envelope to post the migraine and sleep diary back to us at the Department of Psychology, Maynooth University
- Data from the paper and migraine sleep diary will be digitised.

Following this all-paper records will be destroyed. Digitised data will be stored on MU's server following the study (see below).

Follow Up Study:

This a two-part study, you may be invited to participate in part two of the research. As such, we request for your email to contact you about participating **(this is separate from part one and is voluntary)**

- Part two of the study involves an online semi-structured interview, which will last approximately 45 minutes.
- Invitation to part two in no way denotes any clinical or diagnostic significance.
- All email addresses will be kept confidential and destroyed following the study completion. If you are interested in participating and sharing your experience, please provide your email address below.
- Data from the interview will be used to understand the lived experience of migraine and used in a postgraduate research thesis and for publication in academic journals. No personally identifiable data will be used
- Please see below for information on your rights as a participant and data usage

Email: _____

How long will it take?

Time needed daily: (5 minutes)

Time needed after a migraine has occurred: (25 minutes)

Interview: (30 to 45 minutes)

What benefits do I get from participating?

Participation in this study does not lead to any form of medical or psychological diagnosis, and treatment. Information collected from this study is for research purposes only and will not be of any direct clinical use to the individual. It is hoped this study however will provide valuable insight and contribute to existing research on migraine in understanding and treating the disorder. It is anticipated that the results of the study will be published and be available to the public and to participants on request. Participants will also get to keep the Fitbit Inspire 2 supplied

by the Department of Psychology at Maynooth University as a thank you gesture for participating in the study.

What are the risks?

It is possible that you may feel distress when participating due to the studies duration or completing cognitive tasks which are designed to test individuals. If you experience distress, please contact the researcher and avail of the supports provided below.

Data usage:

Data collected from this study will be used for research purposes and academic publication. All data will be stored fully anonymised and unidentifiable for a maximum of 10 years on the MU server as per Maynooth University's Research Integrity guidelines and the European General Data Protection Regulation (GDPR) that came into force since 25th May 2018. Following this 10-year period all data will be destroyed, As Fitbit active watches and mobile app will be used to measure participant actigraphy, participants will have to refer to Fitbit's data usage policy.

Confidentiality:

All data collected will be treated as confidential, in compliance with both University regulations and current statutory provisions, or as required by law. **All data will be held in a fully anonymized format. You will not be personally identified with the data obtained. Only non-identifiable, anonymized data will be held for the 10-year period following completion of the research project as required by the University.** Data will be electronically stored on encrypted PCs and backed up to university secure cloud-based services, accessible only to the researcher and supervisor. It must be recognized that, in some circumstances, confidentiality of research data and records may be overridden by courts in the event of litigation or during investigation by lawful authority. In such circumstances the University will take all reasonable steps within law to ensure that confidentiality is maintained to the greatest possible extent. If during your participation in this study you feel the information and guidelines that you were given have been neglected or disregarded in any way, or if you are unhappy about the process, please contact the Secretary of the Maynooth University Ethics Committee at research.ethics@mu.ie or +353 (0)1 708 6019. Please be assured that your concerns will be dealt with in a sensitive manner.

For your information the Data Controller for this research project is Maynooth University, Maynooth, Co. Kildare. The Data Protection office is located in Room 27, Rye Building, North Campus, Maynooth University, which can be contacted at dataprotection@mu.ie. Maynooth University Data Privacy policies can be found at <https://www.maynoothuniversity.ie/data-protection>.

Research Standards and Rights of Participation:

Participation in this study is voluntary and you may decide not to participate. If you consent to participate now, you may withdraw your data at any time up until the study is completed. Following this all data will be compiled and anonymised for analysis. **This study has been reviewed and received ethical approval by Maynooth University Research Ethics Committee.**

Results from this study:

The research will be written up and presented as part of the researcher's doctoral thesis and presented at national and international conferences and published in scientific journals. A copy of the research findings will be made available to the participant on request.

Contact Information

If you have any questions about participation in this study, please contact the researcher directly.

Researcher Information and Contact: Shannon

Richardson/ shannon.richardson.2017@mumail.ie

Supervisor Information and Contact: Dr Unai Diaz Orueta/

unai.diazorueta@mu.ie

Additional Information

Please note if you are experiencing extreme distress, please contact your general practitioner who can provide you with medical assistance.

Migraine Association of Ireland

For more information on migraine and support please visit [Migraine Association of Ireland: Not Just Another Headache \(https://Migraine.ie/\)](https://Migraine.ie/)

Phone: 01 894 1280/1281

Mobile: 087 149 9798

Information Line: 01 906 1012 (all Ireland)

Phone lines are operated from 10am – 12pm and 2pm – 4pm Tuesday to Friday.

Samaritans

If you are experiencing psychological distress and cannot attend your GP, please contact Samaritans

Phone: 116 123

Phone lines are operated 24 hours a day and it is free to call from both landlines and mobile **Email:** jo@samaritans.org

Appendix D: Consent Form used for Chapter Four, Chapter Five and Chapter Six.

Consent Form

Please tick each statement below:

The purpose and nature of the study have been explained to me in writing. I've been able to ask questions, which were answered satisfactorily. ☐

I am participating voluntarily. ☐

I give permission for my follow-up interview to be audio and video recorded ☐

I understand that I can withdraw from the study, without repercussions, at any time, whether that is before it starts or while I am participating. ☐

I understand that I can withdraw permission to use my data until it is irreversibly anonymised and compiled for analysis following the study. ☐

I understand Fitbit will have access to my actigraphy data. ☐

Signed (Participant)..... Date.....

I the undersigned have taken the time to fully explain to the above participant the nature and purpose of this study in a manner that they could understand. I have explained the risks involved as well as the possible benefits. I have invited them to ask questions on any aspect of the study that concerned them.

Signed (Researcher)..... Date.....

Researcher Name (Block capitals)

If during your participation in this study you feel the information and guidelines that you were given have been neglected or disregarded in any way, or if you are unhappy about the process, please contact the Secretary of the Maynooth University Ethics Committee at research.ethics@mu.ie or +353 (0)1 708 6019. Please be assured that your concerns will be dealt with in a sensitive manner. For your information the Data Controller for this research project is Maynooth University, Maynooth, Co. Kildare. The Data Protection office is located in Room 27, Rye Building, North Campus, Maynooth University, which can be contacted at dataprotection@mu.ie. Maynooth University Data Privacy policies can be found at <https://www.maynoothuniversity.ie/data-protection>.

Please note if you are experiencing extreme distress, please contact your general practitioner who can provide you with medical assistance.

Contact Information:

If you have any questions about participating in this study, please contact the researcher directly.

Researcher Information and Contact: Shannon

Richardson/ shannon.richardson.2017@mumail.ie

Supervisor Information and Contact: Dr Unai Diaz Orueta/

unai.diazorueta@mu.ie

Additional Information

Migraine Association of Ireland

For more information on migraine and support please visit [Migraine Association of Ireland:](https://Migraine.ie/)

[Not Just Another Headache \(https://Migraine.ie/\)](https://Migraine.ie/)

Phone: 01 894 1280/1281

Mobile: 087 149 9798

Information Line: 01 906 1012 (all Ireland)

Phone lines are operated from 10am – 12pm and 2pm – 4pm Tuesday to Friday.

Samaritans:

If you are experiencing psychological distress and cannot attend your GP, please contact Samaritans

Phone: 116 123

Phone lines are operated 24 hours a day and it is free to call from both landlines and mobiles

Email: jo@samaritans.org

Appendix E: Sleep and Migraine Diary used in Chapter Five.

Day: _____ of 90

Date: _____

Have you experienced migraine pain in the last 24 hours? Yes No

***If yes, how long did the pain last?** _____

***What time of day did your migraine pain begin?**

Morning ☐

Afternoon ☐

Evening ☐

Night ☐

***How painful was the migraine?** 1—2—3—4—5—6—7—8—9—10

(Not at all)

(Extremely)

Have you experienced any of the following today?

Unusually increased appetite or snacking Yes No

Unusually reduced appetite Yes No

Felt unusually cold Yes No

Felt unusually warm Yes No

How fatigued have you felt today? 1—2—3—4—5—6—7—8—9—10

(Not at all)

(Extremely)

How unhappy have you felt today? 1—2—3—4—5—6—7—8—9—10

(Not at all)

(Extremely)

How stressed have you felt today? 1—2—3—4—5—6—7—8—9—10

(Not at all)

(Extremely)

What time did you go to bed last night? _____

What time did you try to go to sleep? _____

How long did it take you to fall asleep? _____

How many times did you wake up last night? _____

In total, how long did these awakenings last? _____

What time did you wake up for the day? _____

What time did you get out of bed? _____

Did you wake up earlier or later than planned?

No ☐ Yes, earlier ☐ Yes, later ☐

How would you rate the quality of your sleep?

Very Poor ☐

Poor ☐

Fair ☐

Good ☐

Very Good ☐

Thank you for completing today's migraine and sleep diary. If you experienced a migraine in the last 24-48 hours, please check your email to complete the online psychological tests. This should be completed twice, 24 hours (1 day) and 48 hours (2 days) after a migraine has ended.

Appendix F: Demographic, descriptive and frequency statistics for each participant from Chapter Five.

Table F1. Demographic and descriptive statistics for participant ID3.

ID	Variable	N	Mean	Std. Error
3	Age (years)	1	48.84	0.04
	Pain Duration (minutes)	13	459.23	88.02
	Pain Severity	13	5.38	0.46
	Fatigue	94	5.76	0.15
	Mood	94	4.66	0.14
	Stress	94	4.55	0.16
	Diary Bedtime (hh:mm)	94	23:13	0:06
	Diary Sleep Time (hh:mm)	95	23:39	0:06
	Diary Time to Fall Asleep (h:m)	94	0:16	0:01
	Diary Sleep Onset (hh:mm)	94	23:55	0:05
	Diary Sleep Disturbance Frequency	94	1.06	0.14
	Diary Total Sleep Disturbance Duration (h:m)	94	0:10	0:03
	Diary Wakeup (hh:mm)	94	7:25	0:04
	Diary Getup (hh:mm)	94	8:20	0:04
	Diary Sleep Duration (h:m)	94	7:31	0:06
	Self-reported Sleep Quality	94	4.51	0.09
	Fitbit Sleep Onset (hh:mm)	88	23:43	0:06
	Fitbit Sleep End (hh:mm)	88	8:02	0:06
	Fitbit Sleep Latency (h:m)	88	0:00	0:00
	Fitbit Sleep Duration (h:m)	88	8:18	0:06
	Fitbit Sleep Disturbance (h:m)	88	1:03	0:03
	Fitbit Sleep Inertia (h:m)	88	0:01	0:00
	Fitbit Time in Bed (h:m)	88	8:10	0:07
	Fitbit Sleep Efficiency	88	96.57	0.19
	Fitbit Step Count	91	6266.02	363.34
	Fitbit Resting Heartrate	90	68.84	0.32
	Fitbit Resting Heartrate Error	90	8.11	0.22
	Fitbit Entropy	86	2.53	0.03
	Fitbit Root Mean Square of Successive Differences (RMSSD)	86	24.60	0.75

Table F2. Demographic and descriptive statistics for participant ID4.

ID	Variable	N	Mean	Std. Error
4	Age (years)	1	31.01	0.01
	Pain Duration (minutes)	9	546.67	178.45
	Pain Severity	10	4.80	0.98
	Fatigue	89	3.47	0.26
	Mood	89	2.40	0.19
	Stress	89	1.54	0.08
	Diary Bedtime (hh:mm)	39	23:31	0:08
	Diary Sleep Time (hh:mm)	39	23.89	0:10
	Diary Time to Fall Asleep (h:m)	32	0:19	0:06
	Diary Sleep Onset (hh:mm)	31	24:18	0:14
	Diary Sleep Disturbance Frequency	39	0.01	0.01
	Diary Total Sleep Disturbance Duration (h:m)	39	0:00	0:00
	Diary Wakeup (hh:mm)	41	9:01	0:16
	Diary Getup (hh:mm)	41	9:04	0:16
	Diary Sleep Duration (h:m)	31	8:30	0:16
	Self-reported Sleep Quality	80	3.55	0.07
	Fitbit Sleep Onset (hh:mm)	84	24:08	0:09
	Fitbit Sleep End (hh:mm)	84	8:56	0:10
	Fitbit Sleep Latency (h:m)	84	0.00	0.00
	Fitbit Sleep Duration (h:m)	84	7:44	0:11
	Fitbit Sleep Disturbance (h:m)	84	1:04	0:03
	Fitbit Sleep Inertia (h:m)	84	0:02	0:00
	Fitbit Time in Bed (h:m)	84	8:48	0:13
	Fitbit Sleep Efficiency	84	94.60	0.30
	Fitbit Step Count	82	5839.20	356.32
	Fitbit Resting Heartrate	82	67.15	0.16
	Fitbit Resting Heartrate Error	81	8.30	0.25
	Fitbit Entropy	85	2.27	0.02
	Fitbit Root Mean Square of Successive Differences	85	17.81	0.19

Table F3. Demographic and descriptive statistics for participant ID6.

ID	Variable	N	Mean	Std. Error
6	Age (years)	1	36.00	0.00
	Pain Duration (minutes)	22	837.27	89.98
	Pain Severity	22	5.14	0.37
	Fatigue	90	5.51	0.20
	Mood	90	4.04	0.12
	Stress	90	4.29	0.15
	Diary Bedtime (hh:mm)	90	22:53	0:03
	Diary Sleep Time (hh:mm)	89	23:07	0:03
	Diary Time to Fall Asleep (h:m)	89	0:17	0:01
	Diary Sleep Onset (hh:mm)	89	23:23	0:04
	Diary Sleep Disturbance Frequency	90	2.34	0.12
	Diary Total Sleep Disturbance Duration (h:m)	90	0:25	0:03
	Diary Wakeup (hh:mm)	90	6:37	0:06
	Diary Getup (hh:mm)	90	6:41	0:06
	Diary Sleep Duration (h:m)	90	7:13	0:06
	Self-reported Sleep Quality	90	3.09	0.06
	Fitbit Sleep Onset (hh:mm)	76	23:52	0:07
	Fitbit Sleep End (hh:mm)	76	6:45	0:10
	Fitbit Sleep Latency (h:m)	76	0:01	0:02
	Fitbit Sleep Duration (h:m)	76	6:19	0:09
	Fitbit Sleep Disturbance (h:m)	76	0:40	0:03
	Fitbit Sleep Inertia (h:m)	76	0:01	0:00
	Fitbit Time in Bed (h:m)	76	6:59	0:10
	Fitbit Sleep Efficiency	76	95.59	0.34
	Fitbit Step Count	90	10777.22	334.11
	Fitbit Resting Heartrate	86	61.61	0.21
	Fitbit Resting Heartrate Error	85	9.27	0.45
	Fitbit Entropy	71	2.35	0.02
	Fitbit Root Mean Square of Successive Differences	71	41.09	1.01

Table F4. Demographic and descriptive statistics for participant ID7.

ID	Variable	N	Mean	Std. Error
7	Age (years)	1	45.00	0.00
	Pain Duration (minutes)	3	440.00	40.00
	Pain Severity	5	5.60	0.51
	Fatigue	29	3.03	0.34
	Mood	29	2.17	0.27
	Stress	29	2.69	0.29
	Diary Bedtime (hh:mm)	29	24:25	0:13
	Diary Sleep Time (hh:mm)	29	24:42	0:13
	Diary Time to Fall Asleep (h:m)	28	0:12	0:03
	Diary Sleep Onset (hh:mm)	29	24:51	0:14
	Diary Sleep Disturbance Frequency	29	0.21	0.08
	Diary Total Sleep Disturbance Duration (h:m)	29	0:04	0:03
	Diary Wakeup (hh:mm)	28	8:03	0:12
	Diary Getup (hh:mm)	28	8:03	0:12
	Diary Sleep Duration (h:m)	28	7:12	0:15
	Self-reported Sleep Quality	29	3.10	0.17
	Fitbit Sleep Onset (hh:mm)	29	24:55	0:13
	Fitbit Sleep End (hh:mm)	29	8:12	0:15
	Fitbit Sleep Latency (h:m)	29	0:00	0:00
	Fitbit Sleep Duration (h:m)	29	6:30	0:13
	Fitbit Sleep Disturbance (h:m)	29	0:47	0:03
	Fitbit Sleep Inertia (h:m)	29	0:01	0:00
	Fitbit Time in Bed (h:m)	29	7:16	0:15
	Fitbit Sleep Efficiency	29	94.59	0.38
	Fitbit Step Count	30	10889.93	1028.97
	Fitbit Resting Heartrate	29	64.66	0.56
	Fitbit Resting Heartrate Error	29	8.09	0.85
	Fitbit Entropy	28	2.76	0.04
	Fitbit Root Mean Square of Successive Differences	28	57.07	2.54

Table F5. Demographic and descriptive statistics for participant ID9.

ID	Variable	N	Mean	Std. Error
9	Age (years)	1	32.00	0.00
	Pain Duration (minutes)	29	696.38	66.77
	Pain Severity	31	5.35	0.27
	Fatigue	90	5.38	0.23
	Mood	90	2.82	0.21
	Stress	90	3.70	0.24
	Diary Bedtime (hh:mm)	90	23:33	0:07
	Diary Sleep Time (hh:mm)	90	23:40	0:06
	Diary Time to Fall Asleep (h:m)	88	0:20	0:01
	Diary Sleep Onset (hh:mm)	88	23:59	0:07
	Diary Sleep Disturbance	88	3.68	0.14
	Frequency			
	Diary Total Sleep Disturbance	88	0:55	0:01
	Duration (h:m)			
	Diary Wakeup (hh:mm)	90	8:07	0:09
	Diary Getup (hh:mm)	90	8:17	0:09
	Diary Sleep Duration (h:m)	90	8:09	0:06
	Self-reported Sleep Quality	90	2.84	0.08
	Fitbit Sleep Onset (hh:mm)	88	24:00	0:07
	Fitbit Sleep End (hh:mm)	88	8:12	0:09
	Fitbit Sleep Latency (h:m)	88	0:00	0:00
	Fitbit Sleep Duration (h:m)	88	7:16	0:05
	Fitbit Sleep Disturbance (h:m)	88	0:55	0:01
	Fitbit Sleep Inertia (h:m)	88	0:01	0:00
	Fitbit Time in Bed (h:m)	88	8:12	0:06
	Fitbit Sleep Efficiency	88	94.32	0.24
	Fitbit Step Count	90	6270.66	184.15
	Fitbit Resting Heartrate	89	85.93	0.22
	Fitbit Resting Heartrate Error	89	7.29	0.24
	Fitbit Entropy	88	1.93	0.02
	Fitbit Root Mean Square of Successive Differences	88	12.21	0.22

Table F6. Demographic and descriptive statistics for participant ID10.

ID	Variable	N	Mean	Std. Error
10	Age (years)	1	67.00	0.00
	Pain Duration (minutes)	31	367.74	49.73
	Pain Severity	31	6.23	0.29
	Fatigue	88	6.50	0.17
	Mood	88	4.66	0.19
	Stress	88	4.44	0.15
	Diary Bedtime (hh:mm)	90	23:48	0:11
	Diary Sleep Time (hh:mm)	90	24:07	0:11
	Diary Time to Fall Asleep (h:m)	89	0:23	0:04
	Diary Sleep Onset (hh:mm)	90	24:28	0:12
	Diary Sleep Disturbance Frequency	88	6.66	0.35
	Diary Total Sleep Disturbance Duration (h:m)	90	1:23	0:04
	Diary Wakeup (hh:mm)	90	9:15	0:07
	Diary Getup (hh:mm)	90	9:59	0:07
	Diary Sleep Duration (h:m)	90	8:47	0:12
	Self-reported Sleep Quality	89	3.36	0.08
	Fitbit Sleep Onset (hh:mm)	89	23:51	0:12
	Fitbit Sleep End (hh:mm)	89	10:05	0:09
	Fitbit Sleep Latency (h:m)	89	0:00	0:00
	Fitbit Sleep Duration (h:m)	89	8:49	0:10
	Fitbit Sleep Disturbance (h:m)	89	1:24	0:03
	Fitbit Sleep Inertia (h:m)	89	0:02	0:00
	Fitbit Time in Bed (h:m)	89	10:13	0:20
	Fitbit Sleep Efficiency	89	93.88	0.19
	Fitbit Step Count	90	5166.21	259.85
	Fitbit Resting Heartrate	90	68.48	0.22
	Fitbit Resting Heartrate Error	89	7.42	0.13
	Fitbit Entropy	90	2.66	0.03
	Fitbit Root Mean Square of Successive Differences	90	38.76	0.91

Table F7. Demographic and descriptive statistics for participant ID11.

ID	Variable	N	Mean	Std. Error
11	Age (years)	1	51.00	0.00
	Pain Duration (minutes)	0		
	Pain Severity	0		
	Fatigue	77	4.42	0.21
	Mood	77	2.75	0.11
	Stress	77	2.43	0.10
	Diary Bedtime (hh:mm)	75	23:37	0:04
	Diary Sleep Time (hh:mm)	75	23:48	0:06
	Diary Time to Fall Asleep (h:m)	75	0:33	0:06
	Diary Sleep Onset (hh:mm)	75	24:21	0:08
	Diary Sleep Disturbance	75	4.55	0.27
	Frequency			
	Diary Total Sleep Disturbance	74	0:52	0:04
	Duration (h:m)			
	Diary Wakeup (hh:mm)	75	7:12	0:09
	Diary Getup (hh:mm)	74	7:36	0:07
	Diary Sleep Duration (h:m)	75	6:51	0:11
	Self-reported Sleep Quality	75	2.77	0.11
	Fitbit Sleep Onset (hh:mm)	71	24:28	0:09
	Fitbit Sleep End (hh:mm)	71	7:06	0:10
	Fitbit Sleep Latency (h:m)	74	0:00	0:00
	Fitbit Sleep Duration (h:m)	71	5:43	0:11
	Fitbit Sleep Disturbance (h:m)	71	0:54	0:02
	Fitbit Sleep Inertia (h:m)	71	0:02	0:00
	Fitbit Time in Bed (h:m)	71	6:37	0:12
	Fitbit Sleep Efficiency	71	92.28	0.34
	Fitbit Step Count	48	6403.29	724.12
	Fitbit Resting Heartrate	81	70.06	0.17
	Fitbit Resting Heartrate Error	81	10.00	0.44
	Fitbit Entropy	59	2.23	0.04
	Fitbit Root Mean Square of Successive Differences	59	19.16	0.81

Table F8. Demographic and descriptive statistics for participant ID12.

ID	Variable	N	Mean	Std. Error
12	Age (years)	1	45.00	0.00
	Pain Duration (minutes)	22	422.73	80.47
	Pain Severity	23	5.04	0.51
	Fatigue	89	5.51	0.20
	Mood	89	2.42	0.11
	Stress	88	2.67	0.16
	Diary Bedtime (hh:mm)	90	22:41	0:09
	Diary Sleep Time (hh:mm)	90	23:02	0:09
	Diary Time to Fall Asleep (h:m)	90	0:33	0:02
	Diary Sleep Onset (hh:mm)	90	23:34	0:08
	Diary Sleep Disturbance	90	0.52	0.11
	Frequency			
	Diary Total Sleep Disturbance	90	0:05	0:01
	Duration (h:m)			
	Diary Wakeup (hh:mm)	90	7:40	0:10
	Diary Getup (hh:mm)	90	7:57	0:12
	Diary Sleep Duration (h:m)	90	8:07	0:07
	Self-reported Sleep Quality	90	3.03	0.07
	Fitbit Sleep Onset (hh:mm)	86	23:24	0:09
	Fitbit Sleep End (hh:mm)	86	7:45	0:10
	Fitbit Sleep Latency (h:m)	86	0.00	0.00
	Fitbit Sleep Duration (h:m)	86	7:27	0:07
	Fitbit Sleep Disturbance (h:m)	86	0:54	0:02
	Fitbit Sleep Inertia (h:m)	86	0:01	0:00
	Fitbit Time in Bed (h:m)	86	8:31	0:09
	Fitbit Sleep Efficiency	86	97.22	0.22
	Fitbit Step Count	50	13037.80	636.87
	Fitbit Resting Heartrate	83	62.68	0.33
	Fitbit Resting Heartrate Error	81	2.83	0.03
	Fitbit Entropy	83	8.93	0.40
	Fitbit Root Mean Square of Successive Differences	81	35.67	0.99

Table F9. Demographic and descriptive statistics for participant ID13.

ID	Variable	N	Mean	Std. Error
13	Age (years)	1	63.00	0.00
	Pain Duration (minutes)	39	386.15	40.01
	Pain Severity	41	5.12	0.20
	Fatigue	90	4.58	0.11
	Mood	90	2.12	0.11
	Stress	90	2.82	0.12
	Diary Bedtime (hh:mm)	90	23:09	0:06
	Diary Sleep Time (hh:mm)	90	23:24	0:05
	Diary Time to Fall Asleep (h:m)	90	1:06	0:05
	Diary Sleep Onset (hh:mm)	90	24:30	0:07
	Diary Sleep Disturbance	90	4.50	0.15
	Frequency			
	Diary Total Sleep Disturbance	89	1:09	0:04
	Duration (h:m)			
	Diary Wakeup (hh:mm)	90	7:43	0:07
	Diary Getup (hh:mm)	90	8.:22	0:07
	Diary Sleep Duration (h:m)	90	7:15	0:09
	Self-reported Sleep Quality	90	3.16	0.08
	Fitbit Sleep Onset (hh:mm)	88	23:35	0:07
	Fitbit Sleep End (hh:mm)	88	8:15	0:07
	Fitbit Sleep Latency (h:m)	88	0.00	0.00
	Fitbit Sleep Duration (h:m)	88	7:30	0:07
	Fitbit Sleep Disturbance (h:m)	88	1:10	0:02
	Fitbit Sleep Inertia (h:m)	88	0:07	0:02
	Fitbit Time in Bed (h:m)	88	8:40	0:09
	Fitbit Sleep Efficiency	88	70.68	1.11
	Fitbit Step Count	90	9605.61	272.47
	Fitbit Resting Heartrate	87	65.91	0.22
	Fitbit Resting Heartrate Error	87	1.91	0.03
	Fitbit Entropy	87	7.38	0.14
	Fitbit Root Mean Square of Successive Differences	87	14.80	0.30

Table F10. Demographic and descriptive statistics for participant ID14.

ID	Variable	N	Mean	Std. Error
14	Age (years)	1	32.00	0.00
	Pain Duration (minutes)	1	30.00	.
	Pain Severity	1	4.00	.
	Fatigue	88	6.89	0.20
	Mood	88	3.24	0.16
	Stress	88	2.90	0.16
	Diary Bedtime (hh:mm)	90	23:17	0:05
	Diary Sleep Time (hh:mm)	90	23:44	0:05
	Diary Time to Fall Asleep (h:m)	90	0:59	0:05
	Diary Sleep Onset (hh:mm)	90	24:43	0:07
	Diary Sleep Disturbance	90	28.28	0.76
	Frequency			
	Diary Total Sleep Disturbance	90	0:49	0:01
	Duration (h:m)			
	Diary Wakeup (hh:mm)	90	7:10	0:09
	Diary Getup (hh:mm)	90	8:19	0:07
	Diary Sleep Duration (h:m)	90	7:46	0:06
	Self-reported Sleep Quality	89	2.62	0.12
	Fitbit Sleep Onset (hh:mm)	90	24:43	0:07
	Fitbit Sleep End (hh:mm)	90	7:45	0:07
	Fitbit Sleep Latency (h:m)	90	0:00	0:00
	Fitbit Sleep Duration (h:m)	90	6:12	0:09
	Fitbit Sleep Disturbance (h:m)	90	0:49	0:01
	Fitbit Sleep Inertia (h:m)	90	0:25	0:02
	Fitbit Time in Bed (h:m)	90	7:01	0:09
	Fitbit Sleep Efficiency	90	50.67	0.97
	Fitbit Step Count	59	10646.56	222.57
	Fitbit Resting Heartrate	90	66.77	0.35
	Fitbit Resting Heartrate Error	90	7.14	0.09
	Fitbit Entropy	88	2.74	0.04
	Fitbit Root Mean Square of Successive Differences	88	40.58	1.77

Table F11. Demographic and descriptive statistics for participant ID15.

ID	Variable	N	Mean	Std. Error
15	Age (years)	1	27.00	0.00
	Pain Duration (minutes)	2	420.00	60.00
	Pain Severity	2	6.50	0.50
	Fatigue	90	3.09	0.23
	Mood	90	1.87	0.17
	Stress	90	1.98	0.15
	Diary Bedtime (hh:mm)	90	24:33	0:07
	Diary Sleep Time (hh:mm)	90	24:40	0:07
	Diary Time to Fall Asleep (h:m)	90	0:12	0:01
	Diary Sleep Onset (hh:mm)	90	24:52	0:07
	Diary Sleep Disturbance	90	1.29	0.12
	Frequency			
	Diary Total Sleep Disturbance	90	0:07	0:01
	Duration (h:m)			
	Diary Wakeup (hh:mm)	90	9:28	0:11
	Diary Getup (hh:mm)	89	9:32	0:11
	Diary Sleep Duration (h:m)	90	8:36	0:13
	Self-reported Sleep Quality	90	3.41	0.09
	Fitbit Sleep Onset (hh:mm)	79	24:53	0:07
	Fitbit Sleep End (hh:mm)	79	9:46	0:16
	Fitbit Sleep Latency (h:m)	79	0:00	0:00
	Fitbit Sleep Duration (h:m)	79	7:22	0:12
	Fitbit Sleep Disturbance (h:m)	79	1:12	0:03
	Fitbit Sleep Inertia (h:m)	79	0:01	0:00
	Fitbit Time in Bed (h:m)	79	8:34	0:14
	Fitbit Sleep Efficiency	79	93.63	0.35
	Fitbit Step Count	72	5877.99	390.56
	Fitbit Resting Heartrate	80	68.39	0.42
	Fitbit Resting Heartrate Error	79	7.64	0.21
	Fitbit Entropy	79	2.93	0.03
	Fitbit Root Mean Square of Successive Differences	79	48.05	1.74

Table F12. Demographic and descriptive statistics for participant ID18.

ID	Variable	N	Mean	Std. Error
18	Age (years)	1	63.00	0.00
	Pain Duration (minutes)	25	124.20	8.64
	Pain Severity	30	3.17	0.20
	Fatigue	89	2.88	0.16
	Mood	89	1.74	0.12
	Stress	89	2.12	0.15
	Diary Bedtime (hh:mm)	89	23:42	0:04
	Diary Sleep Time (hh:mm)	88	23:51	0:04
	Diary Time to Fall Asleep (h:m)	88	0:07	0:01
	Diary Sleep Onset (hh:mm)	88	23:58	0:04
	Diary Sleep Disturbance Frequency	88	0.55	0.08
	Diary Total Sleep Disturbance Duration (h:m)	88	0:01	0:04
	Diary Wakeup (hh:mm)	89	6:18	0:06
	Diary Getup (hh:mm)	89	7:28	0:08
	Diary Sleep Duration (h:m)	88	6:20	0:05
	Self-reported Sleep Quality	87	4.60	0.08
	Fitbit Sleep Onset (hh:mm)	89	24:06	0:05
	Fitbit Sleep End (hh:mm)	89	7:10	0:07
	Fitbit Sleep Latency (h:m)	89	0:00	0:00
	Fitbit Sleep Duration (h:m)	89	5:59	0:07
	Fitbit Sleep Disturbance (h:m)	89	1:04	0:02
	Fitbit Sleep Inertia (h:m)	89	0:01	0:00
	Fitbit Time in Bed (h:m)	89	7:04	0:07
	Fitbit Sleep Efficiency	89	92.26	0.26
	Fitbit Step Count	90	13633.41	584.24
	Fitbit Resting Heartrate	90	57.65	0.16
	Fitbit Resting Heartrate Error	89	6.95	0.08
	Fitbit Entropy	89	2.63	0.03
	Fitbit Root Mean Square of Successive Differences	89	29.65	0.55

Table F13. Demographic and descriptive statistics for participant ID19.

ID	Variable	N	Mean	Std. Error
19	Age (years)	1	46.00	0.00
	Pain Duration (minutes)	1	60.00	0
	Pain Severity	19	4.11	0.31
	Fatigue	80	5.05	0.18
	Mood	80	3.44	0.13
	Stress	80	3.04	0.10
	Diary Bedtime (hh:mm)	85	22:16	0:10
	Diary Sleep Time (hh:mm)	88	23:25	0:08
	Diary Time to Fall Asleep (h:m)	84	0:24	0:03
	Diary Sleep Onset (hh:mm)	88	23:44	0:10
	Diary Sleep Disturbance	82	3.32	0.19
	Frequency			
	Diary Total Sleep Disturbance	81	0:04	0:01
	Duration (h:m)			
	Diary Wakeup (hh:mm)	88	7:51	0:08
	Diary Getup (hh:mm)	87	8:10	0:08
	Diary Sleep Duration (h:m)	88	7:56	0:09
	Self-reported Sleep Quality	88	3.57	0.08
	Fitbit Sleep Onset (hh:mm)	84	22:54	0:09
	Fitbit Sleep End (hh:mm)	84	8:04	0:07
	Fitbit Sleep Latency (h:m)	84	0.00	0.00
	Fitbit Sleep Duration (h:m)	84	8:03	0:07
	Fitbit Sleep Disturbance (h:m)	84	1:10	0:03
	Fitbit Sleep Inertia (h:m)	84	0:01	0:00
	Fitbit Time in Bed (h:m)	84	9:13	0:08
	Fitbit Sleep Efficiency	84	95.43	0.23
	Fitbit Step Count	90	9288.38	401.18
	Fitbit Resting Heartrate	89	73.21	0.24
	Fitbit Resting Heartrate Error	88	7.63	0.56
	Fitbit Entropy	85	2.29	0.02
	Fitbit Root Mean Square of Successive Differences	85	30.27	0.61

Table F14. Demographic and descriptive statistics for participant ID22.

ID	Variable	N	Mean	Std. Error
22	Age (years)	1	37.00	0.00
	Pain Duration (minutes)	35	225.43	14.36
	Pain Severity	35	5.40	0.18
	Fatigue	55	6.07	0.16
	Mood	55	4.78	0.16
	Stress	55	4.69	0.17
	Diary Bedtime (hh:mm)	56	24:51	0:13
	Diary Sleep Time (hh:mm)	56	25:16	0:12
	Diary Time to Fall Asleep (h:m)	56	1:11	0:11
	Diary Sleep Onset (hh:mm)	56	26:28	0:15
	Diary Sleep Disturbance	56	2.80	0.19
	Frequency			
	Diary Total Sleep Disturbance	54	0:42	0:03
	Duration (h:m)			
	Diary Wakeup (hh:mm)	55	9:05	0:12
	Diary Getup (hh:mm)	56	9:33	0:10
	Diary Sleep Duration (h:m)	55	6:36	0:14
	Self-reported Sleep Quality	56	2.70	0.08
	Fitbit Sleep Onset (hh:mm)	51	26:36	0:18
	Fitbit Sleep End (hh:mm)	51	8:52	0:15
	Fitbit Sleep Latency (h:m)	51	0:00	0:00
	Fitbit Sleep Duration (h:m)	51	5:31	0:15
	Fitbit Sleep Disturbance (h:m)	51	0:45	0:03
	Fitbit Sleep Inertia (h:m)	51	0:00	0:00
	Fitbit Time in Bed (h:m)	51	6:16	0:17
	Fitbit Sleep Efficiency	51	91.76	0.47
	Fitbit Step Count	59	9481.95	430.66
	Fitbit Resting Heartrate	57	84.81	0.34
	Fitbit Resting Heartrate Error	56	9.70	0.52
	Fitbit Entropy	48	2.08	0.03
	Fitbit Root Mean Square of Successive Differences	48	19.45	0.53

Table F15. Demographic and descriptive statistics for participant ID25.

ID	Variable	N	Mean	Std. Error
25	Age (years)	1	49.00	0.00
	Pain Duration (minutes)	36	828.33	74.52
	Pain Severity	36	5.14	0.25
	Fatigue	90	4.41	0.19
	Mood	90	2.78	0.14
	Stress	90	3.10	0.13
	Diary Bedtime (hh:mm)	90	24:21	0:11
	Diary Sleep Time (hh:mm)	90	24:16	0:11
	Diary Time to Fall Asleep (h:m)	90	0.26	0:01
	Diary Sleep Onset (hh:mm)	90	24:33	0:11
	Diary Sleep Disturbance	90	2.38	0.16
	Frequency			
	Diary Total Sleep Disturbance	90	0:53	0:03
	Duration (h:m)			
	Diary Wakeup (hh:mm)	90	8:48	0:12
	Diary Getup (hh:mm)	90	8:55	0:12
	Diary Sleep Duration (h:m)	90	8:15	0:10
	Self-reported Sleep Quality	90	3.07	0.08
	Fitbit Sleep Onset (hh:mm)	86	24:39	0:11
	Fitbit Sleep End (hh:mm)	86	8:59	0:12
	Fitbit Sleep Latency (h:m)	86	0:00	0:00
	Fitbit Sleep Duration (h:m)	86	7:08	0:10
	Fitbit Sleep Disturbance (h:m)	86	0:55	0:03
	Fitbit Sleep Inertia (h:m)	86	0:13	0:01
	Fitbit Time in Bed (h:m)	86	8:03	0:10
	Fitbit Sleep Efficiency	86	64.48	0.89
	Fitbit Step Count	88	10599.52	515.27
	Fitbit Resting Heartrate	89	65.03	0.24
	Fitbit Resting Heartrate Error	89	7.44	0.15
	Fitbit Entropy	83	2.43	0.03
	Fitbit Root Mean Square of Successive Differences	83	17.10	0.34

Table F16. Frequency statistics for Participant ID3.

ID	Variable	N	Percentage
3			
	Non-Migraine Days	81	85.3%
	Migraine Days	13	13.7%
	Morning Onset Migraine	11	84.6%
	Afternoon Onset Migraine	1	7.7%
	Evening Onset Migraine	1	7.7%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	11	11.6%
	<i>No</i>	82	86.3%
	Decreased Appetite		
	<i>Yes</i>	8	8.4%
	<i>No</i>	85	89.5%
	Felt Unusually Cold		
	<i>Yes</i>	13	13.7%
	<i>No</i>	80	84.2%
	Felt Unusually Warm		
	<i>Yes</i>	4	4.2%
	<i>No</i>	89	93.7%
	Woke up early or later than planned		
	<i>No</i>	56	58.9%
	<i>Yes, earlier</i>	34	35.8%
	<i>Yes, later</i>	4	4.2%

Table F17. Frequency statistics for Participant ID4.

ID	Variable	N	Frequency
4	Non-Migraine Days	77	85.6%
	Migraine Days	12	13.3%
	Morning Onset Migraine	4	33.3%
	Afternoon Onset Migraine	4	33.3%
	Evening Onset Migraine	3	25%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	1	1.1%
	<i>No</i>	82	91.1%
	Decreased Appetite		
	<i>Yes</i>	1	1.1%
	<i>No</i>	83	92.2%
	Felt Unusually Cold		
	<i>Yes</i>	4	4.4%
	<i>No</i>	80	88.9%
	Felt Unusually Warm		
	<i>Yes</i>	0	0%
	<i>No</i>	84	93.3%
	Woke up early or later than planned		
	<i>No</i>	51	56.7%
	<i>Yes, earlier</i>	0	0%
	<i>Yes, later</i>	13	28.9%

Table F18. Frequency statistics for Participant ID6.

ID	Variable	N	Frequency
6	Non-Migraine Days	68	51.5%
	Migraine Days	22	16.7%
	Morning Onset Migraine	9	40.9%
	Afternoon Onset Migraine	13	59.1%
	Evening Onset Migraine	0	0%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	26	19.7%
	<i>No</i>	64	48.5%
	Decreased Appetite		
	<i>Yes</i>	2	1.5%
	<i>No</i>	88	66.7%
	Felt Unusually Cold		
	<i>Yes</i>	23	17.4%
	<i>No</i>	67	50.8%
	Felt Unusually Warm		
	<i>Yes</i>	4	3.0%
	<i>No</i>	86	65.2%
	Woke up early or later than planned		
	<i>No</i>	36	27.3%
	<i>Yes, earlier</i>	53	40.2%
	<i>Yes, later</i>	1	0.8%

Table F19. Frequency statistics for Participant ID7.

ID	Variable	N	Frequency
7	Non-Migraine Days	25	83.3%
	Migraine Days	5	16.7%
	Morning Onset Migraine	4	80%
	Afternoon Onset Migraine	0	0%
	Evening Onset Migraine	0	0%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	6	20%
	<i>No</i>	22	73.3%
	Decreased Appetite		
	<i>Yes</i>	3	10%
	<i>No</i>	25	83.3%
	Felt Unusually Cold		
	<i>Yes</i>	2	6.7%
	<i>No</i>	27	90%
	Felt Unusually Warm		
	<i>Yes</i>	8	26.7%
	<i>No</i>	21	70%
	Woke up earlier or later than planned		
	<i>No</i>	15	50%
	<i>Yes, earlier</i>	1	3.3%
	<i>Yes, later</i>	12	40%

Table F20. Frequency statistics for Participant ID9.

ID	Variable	N	Frequency
9	Non-Migraine Days	59	65.6%
	Migraine Days	31	34.4%
	Morning Onset Migraine	17	54.8%
	Afternoon Onset Migraine	6	19.4%
	Evening Onset Migraine	6	19.4%
	Night Onset Migraine	2	6.5%
	Increased Appetite		
	<i>Yes</i>	8	8.9%
	<i>No</i>	82	91.1%
	Decreased Appetite		
	<i>Yes</i>	0	0%
	<i>No</i>	90	100%
	Felt Unusually Cold		
	<i>Yes</i>	11	12.2%
	<i>No</i>	79	87.8%
	Felt Unusually Warm		
	<i>Yes</i>	0	0%
	<i>No</i>	90	100%
	Woke up earlier or later than planned		
	<i>No</i>	52	57.8%
	<i>Yes, earlier</i>	18	20%
	<i>Yes, later</i>	20	22.2%

Table F21. Frequency statistics for Participant ID10

ID	Variable	N	Frequency
10	Non-Migraine Days	57	63.3%
	Migraine Days	31	34.4%
	Morning Onset Migraine	11	35.5%
	Afternoon Onset Migraine	9	29%
	Evening Onset Migraine	7	22.6%
	Night Onset Migraine	3	9.7%
	Increased Appetite		
	<i>Yes</i>	18	20%
	<i>No</i>	69	76.7%
	Decreased Appetite		
	<i>Yes</i>	6	6.7%
	<i>No</i>	81	90%
	Felt Unusually Cold		
	<i>Yes</i>	26	28.9%
	<i>No</i>	61	67.8%
	Felt Unusually Warm		
	<i>Yes</i>	3	3.3%
	<i>No</i>	84	93.3%
	Woke up earlier or later than planned		
	<i>No</i>	42	46.7%
	<i>Yes, earlier</i>	6	6.7%
	<i>Yes, later</i>	41	45.6%

Table F22. Frequency statistics for Participant ID11.

ID	Variable	N	Frequency
11	Non-Migraine Days	77	93.9%
	Migraine Days	0	0%
	Morning Onset Migraine	0	0%
	Afternoon Onset Migraine	0	0%
	Evening Onset Migraine	0	0%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	2	2.4%
	<i>No</i>	75	91.5%
	Decreased Appetite		
	<i>Yes</i>	0	0%
	<i>No</i>	77	93.9%
	Felt Unusually Cold		
	<i>Yes</i>	3	3.7%
	<i>No</i>	74	90.2%
	Felt Unusually Warm		
	<i>Yes</i>	8	9.8%
	<i>No</i>	69	84.1%
	Woke up early or later than planned		
	<i>No</i>	33	40.2%
	<i>Yes, earlier</i>	39	47.6%
	<i>Yes, later</i>	3	3.7%

Table F23. Frequency statistics for Participant ID12.

ID	Variable	N	Frequency
12	Non-Migraine Days	66	73.3%
	Migraine Days	24	26.7%
	Morning Onset Migraine	17	70.8%
	Afternoon Onset Migraine	6	25%
	Evening Onset Migraine	1	4.2%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	0	0%
	<i>No</i>	90	100%
	Decreased Appetite		
	<i>Yes</i>	4	4.4%
	<i>No</i>	86	95.6%
	Felt Unusually Cold		
	<i>Yes</i>	9	10%
	<i>No</i>	81	90%
	Felt Unusually Warm		
	<i>Yes</i>	12	13.3%
	<i>No</i>	78	86.7%
	Woke up early or later than planned		
	<i>No</i>	81	90%
	<i>Yes, earlier</i>	4	4.4%
	<i>Yes, later</i>	5	5.6%

Table F24. Frequency statistics for Participant ID13.

ID	Variable	N	Frequency
13	Non-Migraine Days	49	54.4%
	Migraine Days	41	45.6%
	Morning Onset Migraine	7	17.1%
	Afternoon Onset Migraine	25	61%
	Evening Onset Migraine	5	12.2%
	Night Onset Migraine	4	9.8%
	Increased Appetite		
	<i>Yes</i>	40	44.4%
	<i>No</i>	49	54.4%
	Decreased Appetite		
	<i>Yes</i>	2	2.2%
	<i>No</i>	87	96.7%
	Felt Unusually Cold		
	<i>Yes</i>	15	16.7%
	<i>No</i>	74	82.2%
	Felt Unusually Warm		
	<i>Yes</i>	2	2.2%
	<i>No</i>	87	96.7%
	Woke up early or later than planned		
	<i>No</i>	46	51.1%
	<i>Yes, earlier</i>	43	47.8%
	<i>Yes, later</i>	0	0%

Table F25. Frequency statistics for Participant ID14.

ID	Variable	N	Frequency
14	Non-Migraine Days	88	97.8%
	Migraine Days	1	1.1%
	Morning Onset Migraine	1	100%
	Afternoon Onset Migraine	0	0%
	Evening Onset Migraine	0	0%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	34	37.8%
	<i>No</i>	53	58.9%
	Decreased Appetite		
	<i>Yes</i>	0	0%
	<i>No</i>	87	96.7%
	Felt Unusually Cold		
	<i>Yes</i>	29	32.2%
	<i>No</i>	58	64.4%
	Felt Unusually Warm		
	<i>Yes</i>	2	2.2%
	<i>No</i>	85	94.4%
	Woke up early or later than planned		
	<i>No</i>	51	56.7%
	<i>Yes, earlier</i>	39	43.3%
	<i>Yes, later</i>	0	0%

Table F26. Frequency statistics for Participant ID15

1D	Variable	N	Frequency
15	Non-Migraine Days	87	96.7%
	Migraine Days	3	3.3%
	Morning Onset Migraine	0	0%
	Afternoon Onset Migraine	1	33.3%
	Evening Onset Migraine	1	33.3%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	13	14.4%
	<i>No</i>	77	85.6%
	Decreased Appetite		
	<i>Yes</i>	15	16.7%
	<i>No</i>	75	83.3%
	Felt Unusually Cold		
	<i>Yes</i>	21	23.3%
	<i>No</i>	69	76.7%
	Felt Unusually Warm		
	<i>Yes</i>	1	1.1%
	<i>No</i>	89	98.9%
	Woke up earlier or later than planned		
	<i>No</i>	59	65.6%
	<i>Yes, earlier</i>	10	11.1%
	<i>Yes, later</i>	21	23.3%

Table F27. Frequency statistics for Participant ID18.

ID	Variable	N	Frequency
18	Non-Migraine Days	60	66.7%
	Migraine Days	30	33.3%
	Morning Onset Migraine	11	36.7%
	Afternoon Onset Migraine	14	46.7%
	Evening Onset Migraine	5	16.7%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	0	0%
	<i>No</i>	88	97.8%
	Decreased Appetite		
	<i>Yes</i>	0	0%
	<i>No</i>	89	98.9%
	Felt Unusually Cold		
	<i>Yes</i>	0	0%
	<i>No</i>	89	98.9%
	Felt Unusually Warm		
	<i>Yes</i>	0	0%
	<i>No</i>	89	98.9%
	Woke up early or later than planned		
	<i>No</i>	55	61.1%
	<i>Yes, earlier</i>	23	25.6%
	<i>Yes, later</i>	9	10%

Table F28. Frequency statistics for Participant ID19.

ID	Variable	N	Frequency
19	Non-Migraine Days	63	70%
	Migraine Days	19	21.1%
	Morning Onset Migraine	8	42.1%
	Afternoon Onset Migraine	4	21.1%
	Evening Onset Migraine	7	36.8%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	11	12.2%
	<i>No</i>	68	75.6%
	Decreased Appetite		
	<i>Yes</i>	18	20%
	<i>No</i>	61	67.8%
	Felt Unusually Cold		
	<i>Yes</i>	25	27.8%
	<i>No</i>	54	60%
	Felt Unusually Warm		
	<i>Yes</i>	8	8.9%
	<i>No</i>	71	78.9%
	Woke up early or later than planned		
	<i>No</i>	51	56.7%
	<i>Yes, earlier</i>	23	25.6%
	<i>Yes, later</i>	14	15.6%

Table F29. Frequency statistics for Participant ID22.

ID	Variable	N	Frequency
22	Non-Migraine Days	21	35.6%
	Migraine Days	35	59.3%
	Morning Onset Migraine	18	51.4%
	Afternoon Onset Migraine	16	45.7%
	Evening Onset Migraine	1	2.9%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	12	20.3%
	<i>No</i>	36	61%
	Decreased Appetite		
	<i>Yes</i>	1	1.7%
	<i>No</i>	47	79.7%
	Felt Unusually Cold		
	<i>Yes</i>	8	13.6%
	<i>No</i>	40	67.8%
	Felt Unusually Warm		
	<i>Yes</i>	8	13.6%
	<i>No</i>	40	67.8%
	Woke up earlier or later than planned		
	<i>No</i>	14	23.7%
	<i>Yes, earlier</i>	21	35.6%
	<i>Yes, later</i>	21	35.6%

Table F30. Frequency statistics for Participant ID25.

ID	Variable	N	Frequency
25	Non-Migraine Days	54	60%
	Migraine Days	36	40%
	Morning Onset Migraine	26	72.2%
	Afternoon Onset Migraine	7	19.4%
	Evening Onset Migraine	3	8.3%
	Night Onset Migraine	0	0%
	Increased Appetite		
	<i>Yes</i>	11	12.2%
	<i>No</i>	79	87.8%
	Decreased Appetite		
	<i>Yes</i>	9	10%
	<i>No</i>	81	90%
	Felt Unusually Cold		
	<i>Yes</i>	11	12.2%
	<i>No</i>	79	87.8%
	Felt Unusually Warm		
	<i>Yes</i>	9	10%
	<i>No</i>	81	90.9%
	Woke up earlier or later than planned		
	<i>No</i>	51	56.7%
	<i>Yes, earlier</i>	13	14.4%
	<i>Yes, later</i>	26	28.9%

Appendix G: Additional models of omitted variables from Chapter Five.

Backward Visual Digit Span

A Bayesian Poisson regression model was used to examine the dependent variable backward two error maximum length (BTEML) with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model indicted no effects of the predictor variables on BTEML scores. Pairwise comparisons revealed reduced BTEML scores in session 1 compared to session 5 (95% HPD CrI = [0.47, 0.89], IRR = .67).

A Bayesian negative binomial regression model was used to examine the dependent variable backward two error total trials (BTETT) with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from this model indicated a positive effect of Session 5 (48 hours after migraine two; l-95% CI = 0.17, u-95% CI = 0.82) compared to BTETT scores in the reference level, session 1. Pairwise comparisons revealed reduced BTETT scores in session 1 and session 2 compared to session 5. Greater BTETT scores were observed in session 5 compared to session 6 and 8 (see table D1).

Table G1. Table displaying significant differences from pairwise comparisons of backward error total trials between sessions. Significance determined by 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 48hrs after migraine 2 (Session 1 / Session 3)	0.60	0.421	0.82
24hrs after migraine 1 / 48hrs after migraine 2 (Session 2 / Session 5)	0.70	0.481	0.94
48hrs after migraine 2 / 24hrs after migraine 3 (Session 5 / Session 6)	1.50	1.02	2.14
48hrs after migraine 2 / Baseline 2 (Session 5 / Session 8)	1.44	1.03	1.97

Go No-Go

A Bayesian beta regression model was used to examine the dependent variable error rate in trials with the vertical cue with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model suggested that there were no effects of the predictor variables on error rate in vertical cue trials. Pairwise comparisons revealed reduced error rates in the vertical cue trials in session 2 compared to session 3 (95% HPD CrI = [0.09, 0.71], MR = 0.78).

A Bayesian beta regression model was used to examine the dependent variable error rate in trials with the horizontal cue with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via

posterior predictive checks. Results from the model indicated no effects of the predictor variables on error rate in horizontal cue trials. Pairwise comparisons revealed no differences in error rate in horizontal cue trials between session levels.

A Bayesian beta regression model was used to examine the dependent variable omission error rate in trials presented with the vertical cue with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model suggested no effects of the predictor variables on omission error rate with the vertical cue. Pairwise comparisons revealed reduced omission error rate in vertical cue trials in session 2 compared to session 3 (95% HPD CrI = [0.11, 0.86], MR = 0.38)

A Bayesian beta regression model was used to examine the dependent variable commission error rate in trials presented with the vertical cue with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model suggested there were no effects of the predictor variables on commission error rate with the vertical cue. Pairwise comparisons revealed reduced commission error rate in vertical cue trials in session 1 and session 2 compared to session 3 (see table F2).

Table G2. Table displaying significant differences from pairwise comparisons of commission error rate in vertical cue trials between sessions. Significance determined from 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 48hrs after migraine 1 (Session 1 / Session 3)	0.41	0.12	0.93
24hrs after migraine 1 / 48hrs after migraine 1 (Session 2 / Session 3)	0.27	0.07	0.67

A Bayesian beta regression model was used to examine the dependent variable omission error rate in trials with the horizontal cue with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model suggested there were no effects of the predictor variables on omission error rate with the horizontal cue. Pairwise comparisons further revealed no differences in omission error rate in horizontal cue trials between session levels.

A Bayesian beta regression model was used to examine the dependent variable commission error rate in trials with the horizontal cue with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model suggested there were no effects of the predictor variables on commission error rate with the horizontal cue. Pairwise comparisons further revealed no differences in commission error rate in horizontal cue trials between session levels.

A Bayesian gamma regression model was used to examine the dependent variable mean reaction times in go trials with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results from the model indicated a negative effect of session 3 on mean reaction time in go trials in the reference session 1 (95% CrI = [-0.22, -0.01]). Pairwise comparisons revealed greater mean reaction times in go trials in session 1 (baseline) compared to session 3. Reduced reaction times in go trials were observed in session 3 compared sessions 4, 5 and 7 (see table F3).

Table G3. Table displaying significant differences from pairwise comparisons of mean reaction times in go trials between sessions. Significance determined from 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
Baseline / 48hrs after migraine 1 (Session 1 / Session 3)	1.12	1.01	1.24
48hrs after migraine 1 / 24hrs after migraine 2 (Session 3 / Session 4)	0.85	0.76	0.95
48hrs after migraine 1 / 48hrs after migraine 2 (Session 3 / Session 5)	0.88	0.78	0.99
48hrs after migraine 1 / 48hrs after migraine 3 (Session 3 / Session 7)	0.87	0.76	0.98

A Bayesian gamma regression model was used to examine the dependent variable mean reaction times in go trials with the vertical cue with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results indicated that there were no effects

of the predictor variables on reaction time to go trials using the vertical cue. Pairwise comparisons revealed reduced reaction times in go trials with the vertical cue in session 3 (48 hours after migraine 1) compared to session 4 (24 hours after migraine 2; 95% HPD CrI = [0.79, 0.99], MR = 0.89).

A Bayesian gamma regression model was used to examine the dependent variable mean reaction times in go trials with the horizontal cue with session as the primary predictor and age, migraine type and employment as covariates. A random intercept for participant was also included in the model. Model adequacy was assessed via posterior predictive checks. Results indicated that there were no effects of the predictor variables on reaction time to go trials using the horizontal cue. Pairwise comparisons revealed reduced reaction time in go trials using the horizontal cue in session 3 (48 hours after migraine 1) compared to sessions 4, 5 and 7 (see Table F4).

Table G4. Table displaying significant differences from pairwise multiple comparisons of mean reaction times in go trials with the horizontal cue between sessions. Significance determined from 95% Highest Posterior Density (HPD) intervals.

Contrast	Odds Ratio	Lower. HPD	Upper. HPD
48hrs after migraine 1 / 24hrs after migraine 2 (Session 3 / Session 4)	0.87	0.76	0.97
48hrs after migraine 1 / 48hrs after migraine 2 (Session 3 / Session 5)	0.85	0.74	0.96
48hrs after migraine 1 / 48hrs after migraine 3 (Session 3 / Session 7)	0.87	0.76	0.99

Appendix H: Line plots of variables included in Chapter Five.

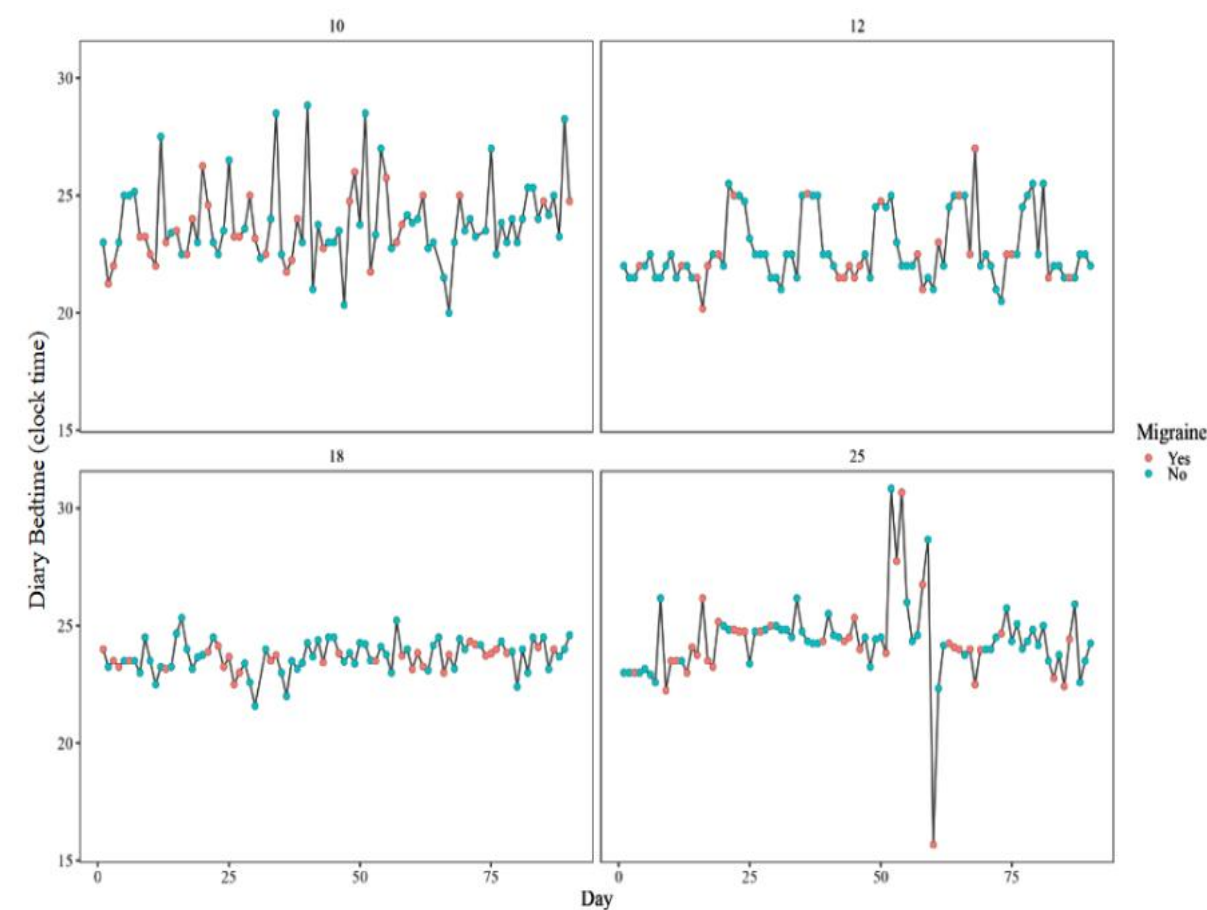


Figure H1. Line plots of diary bedtime scores of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

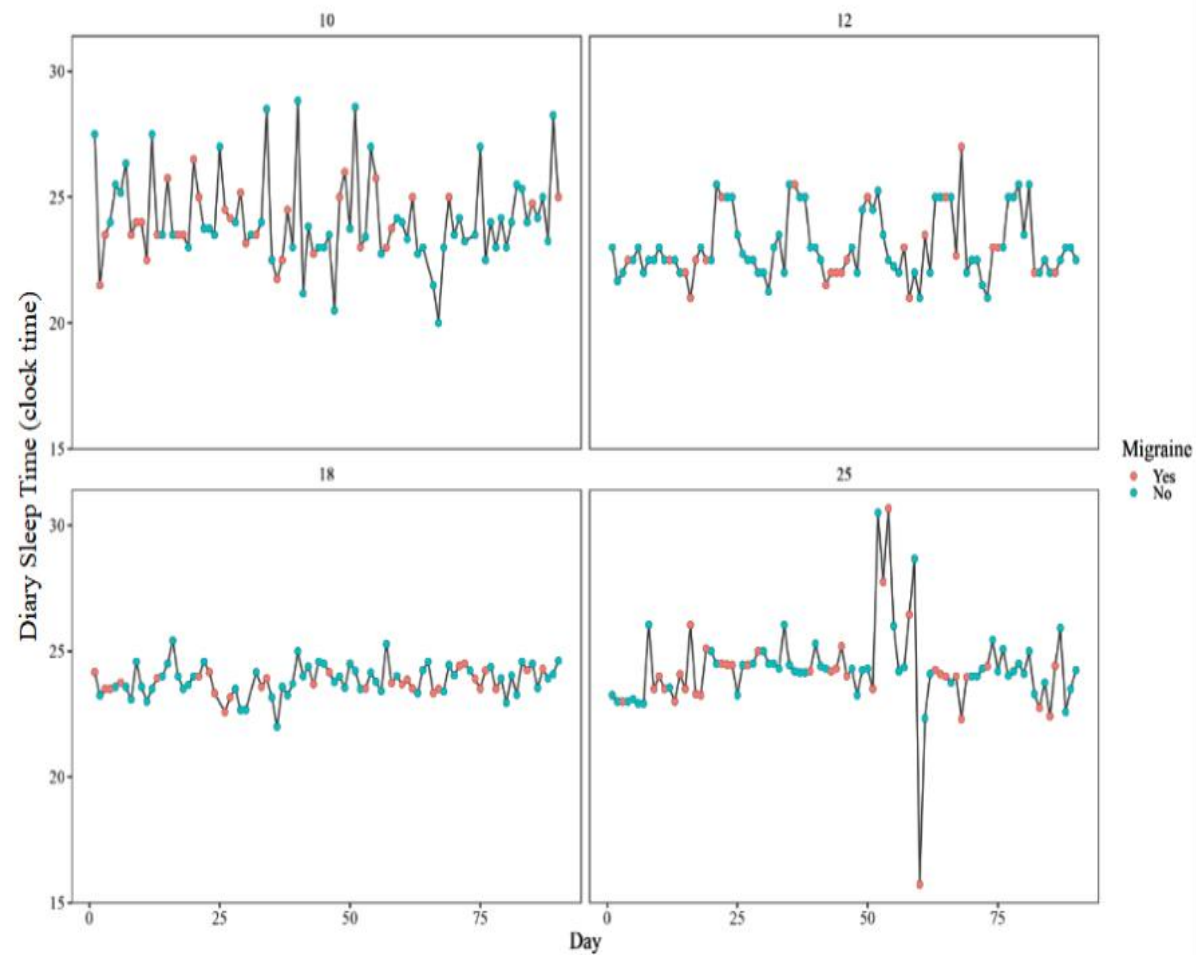


Figure H2. Line plots of diary sleep time scores of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

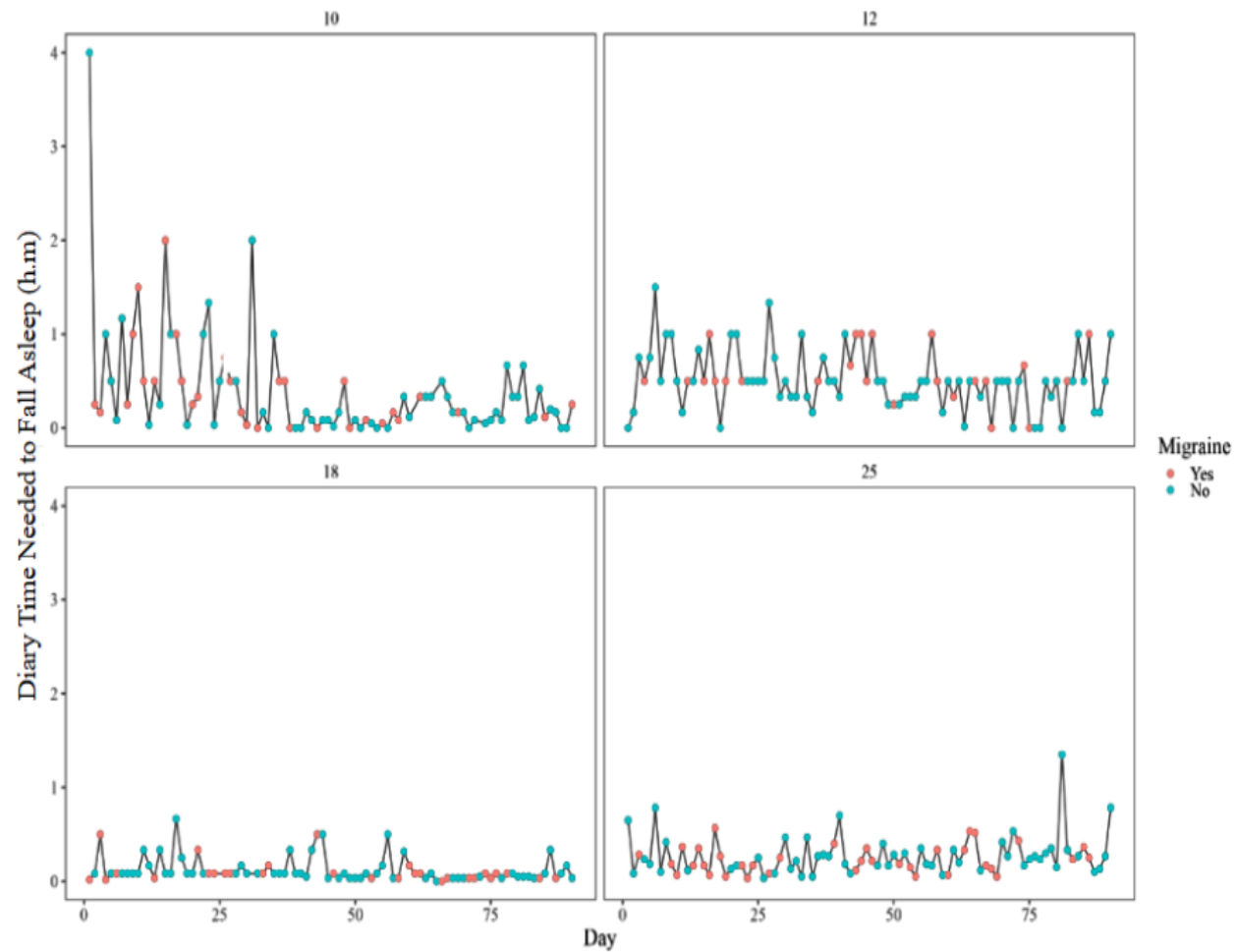


Figure H3. Line plots of diary time needed to fall asleep scores from four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

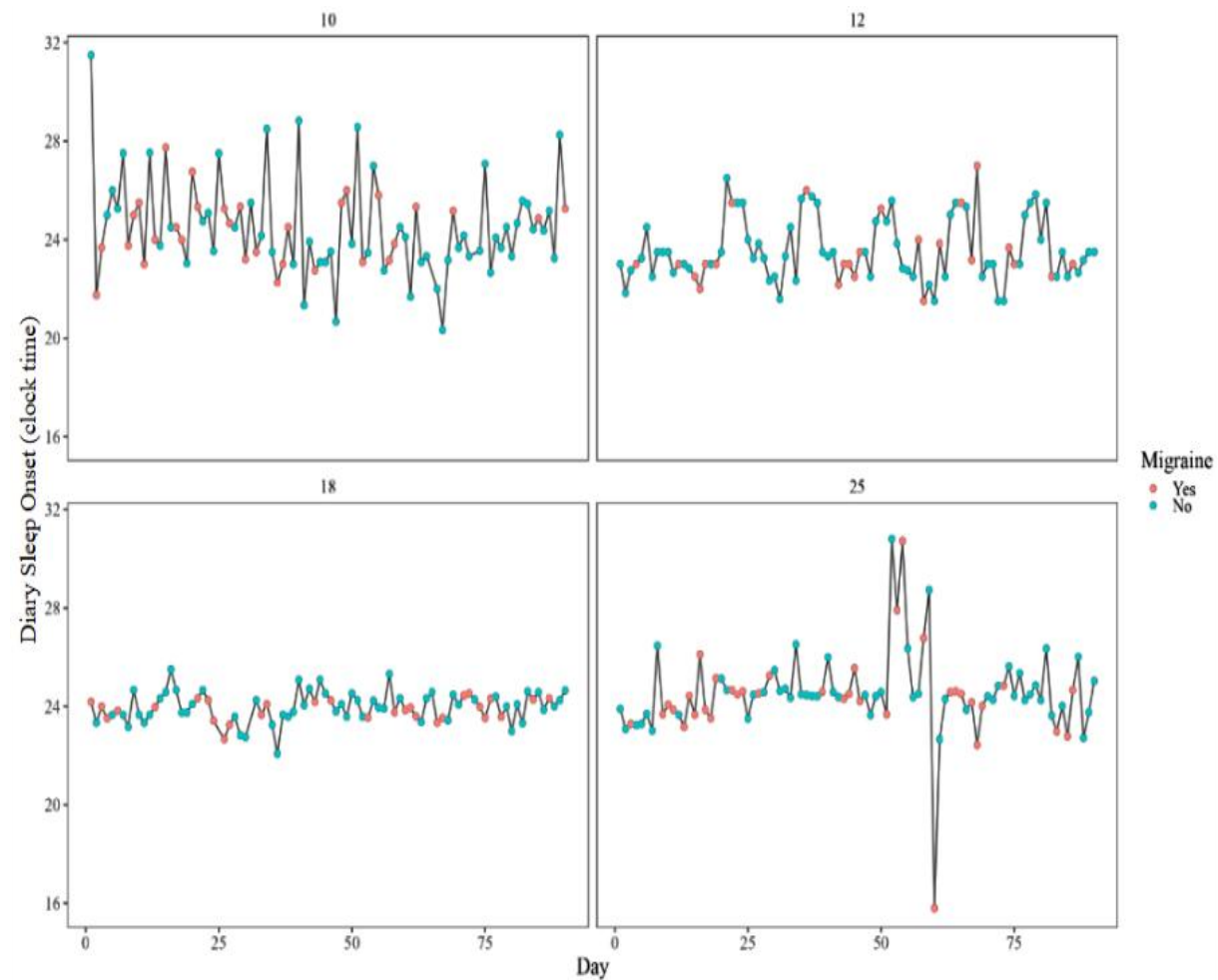


Figure H4. Line plots of diary sleep onset scores of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

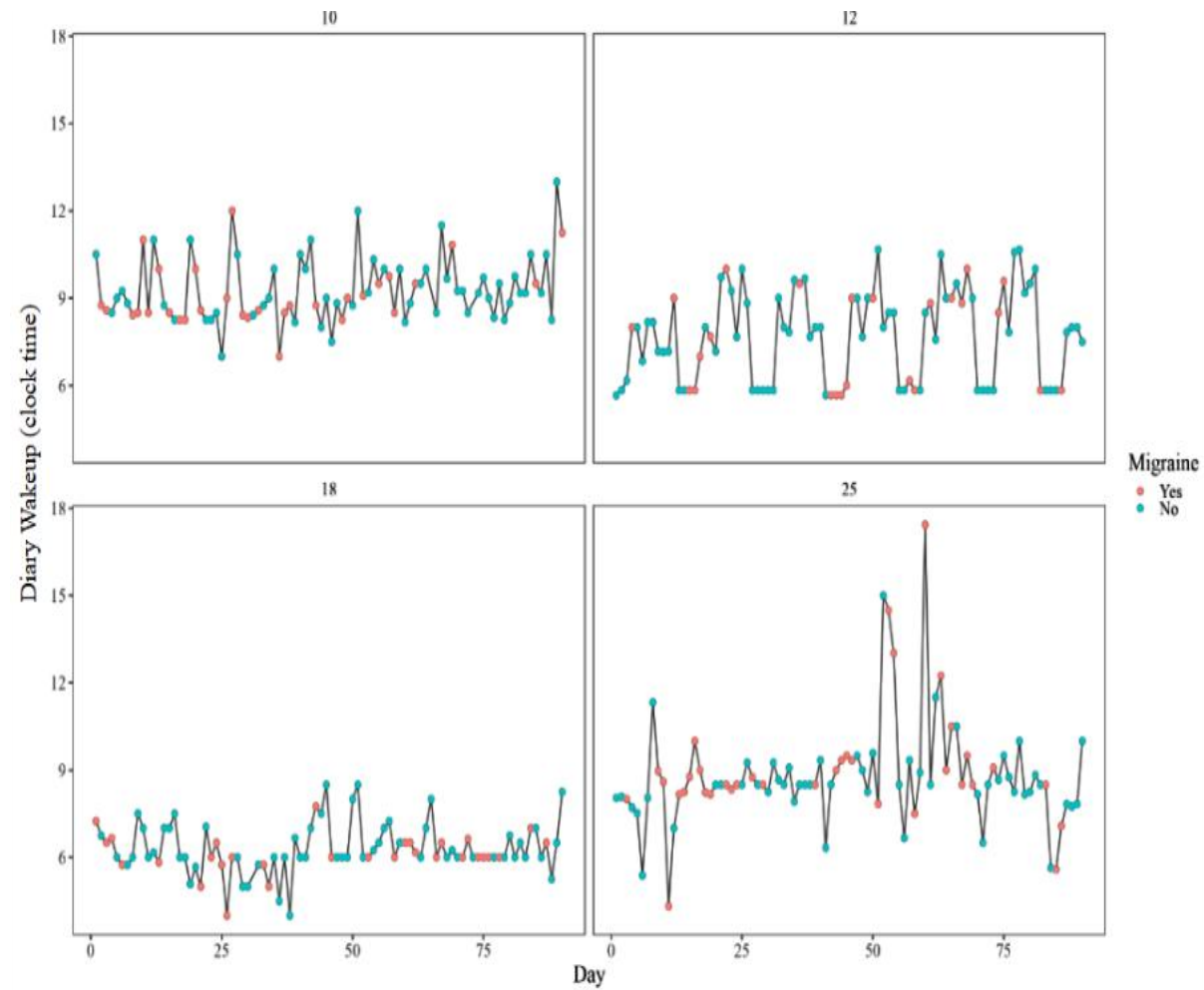


Figure H5. Line plots of diary sleep disturbance frequency of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

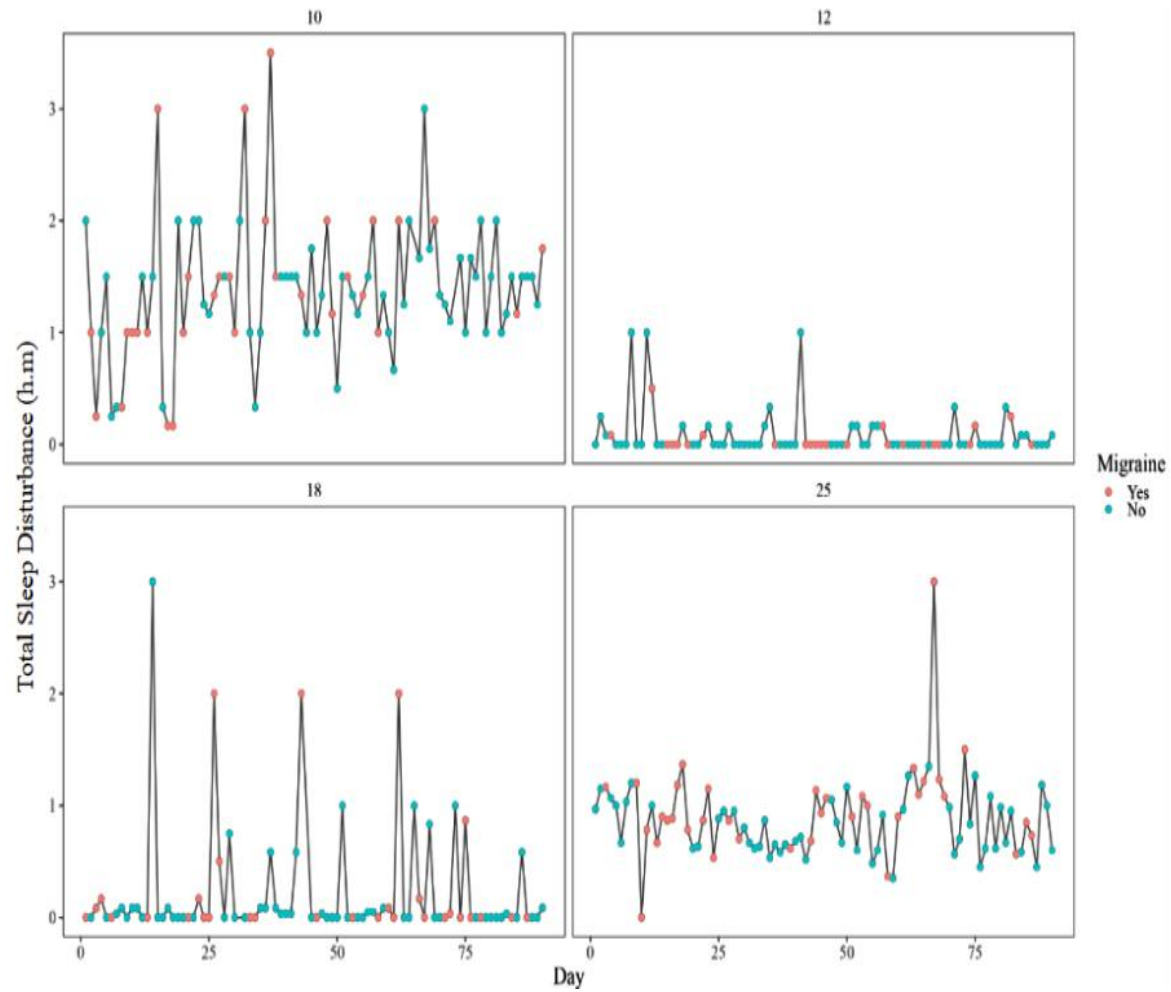


Figure H6. Line plots of diary sleep disturbance duration (h.m) of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

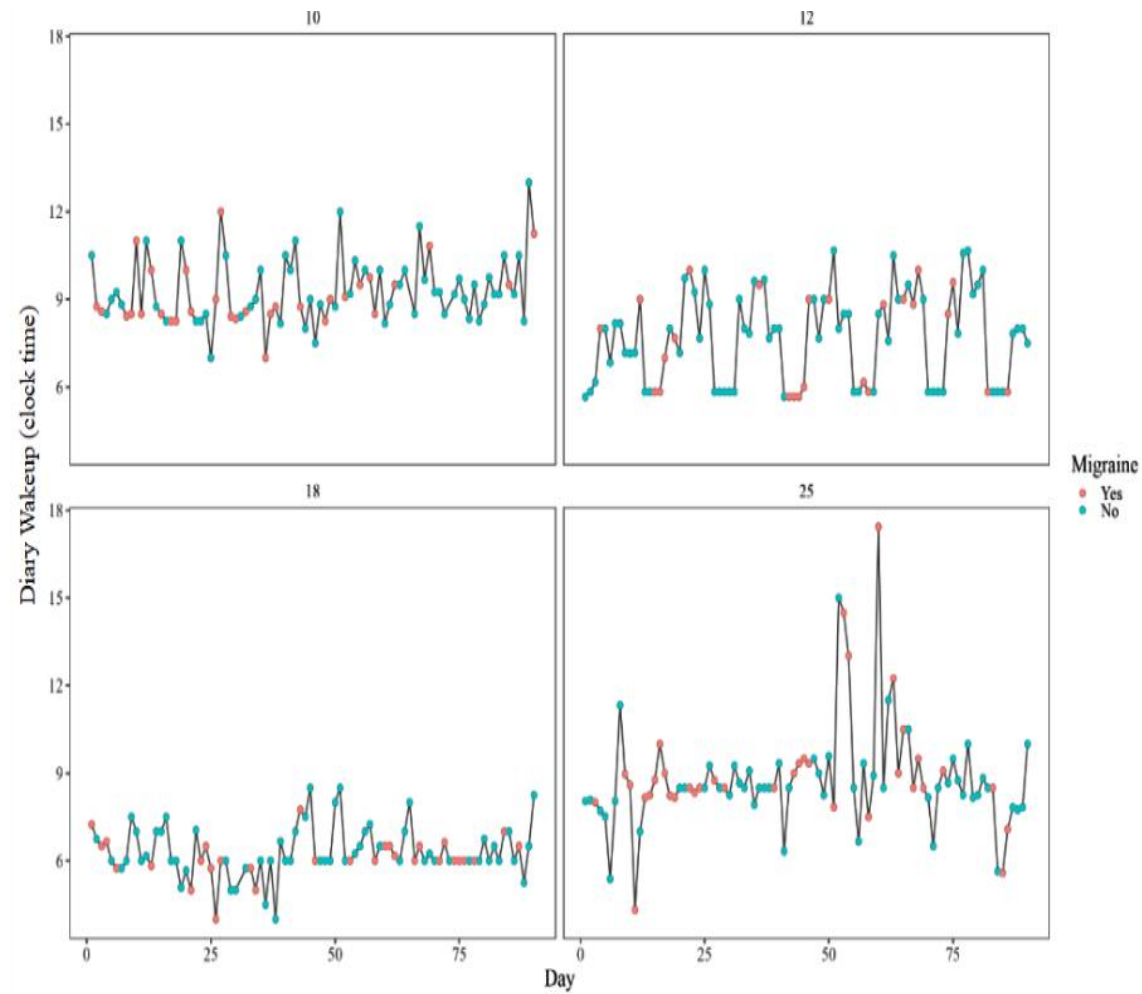


Figure H7. Line plots of diary wake up time of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

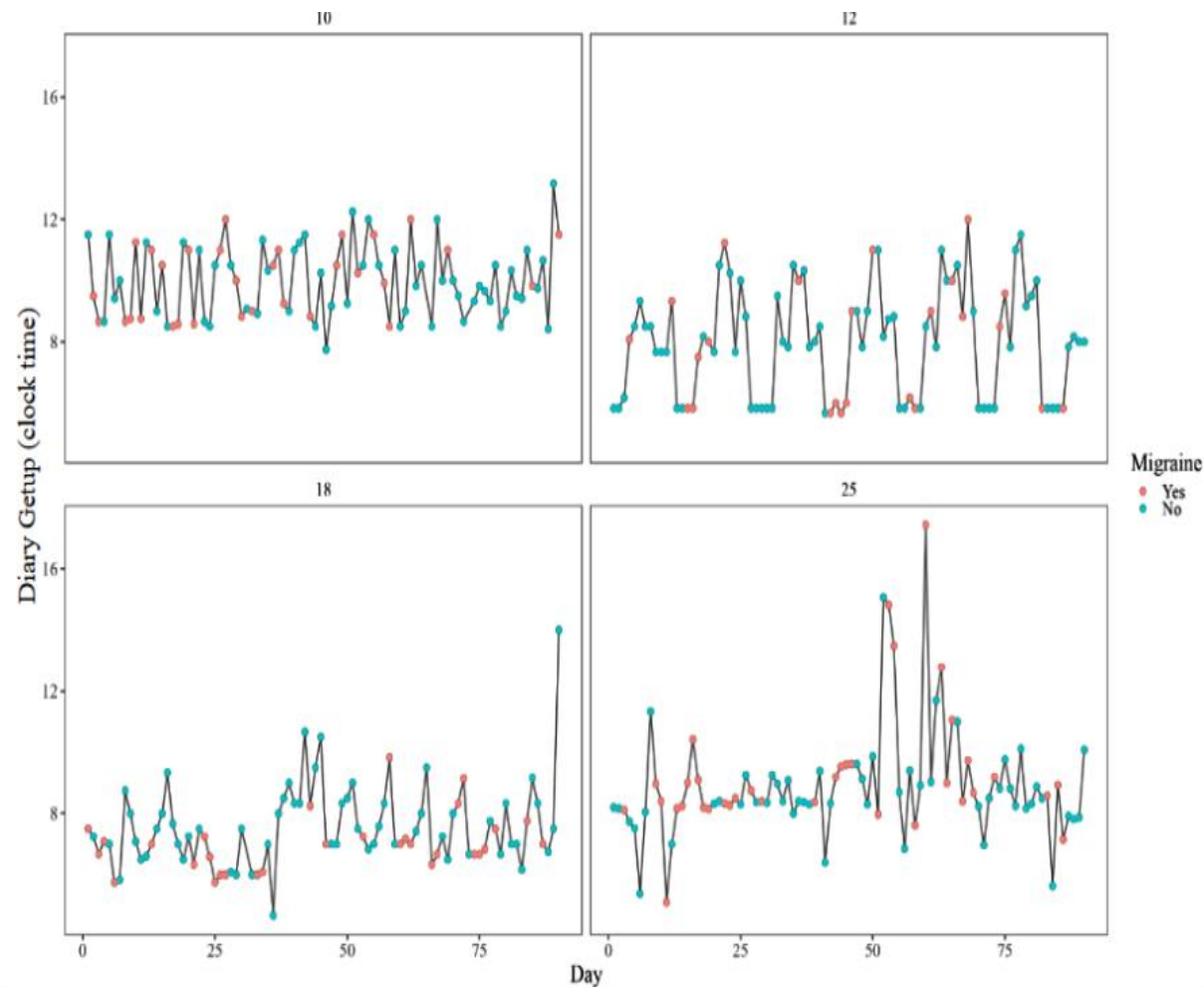


Figure H8. Line plots of Diary Getup time of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

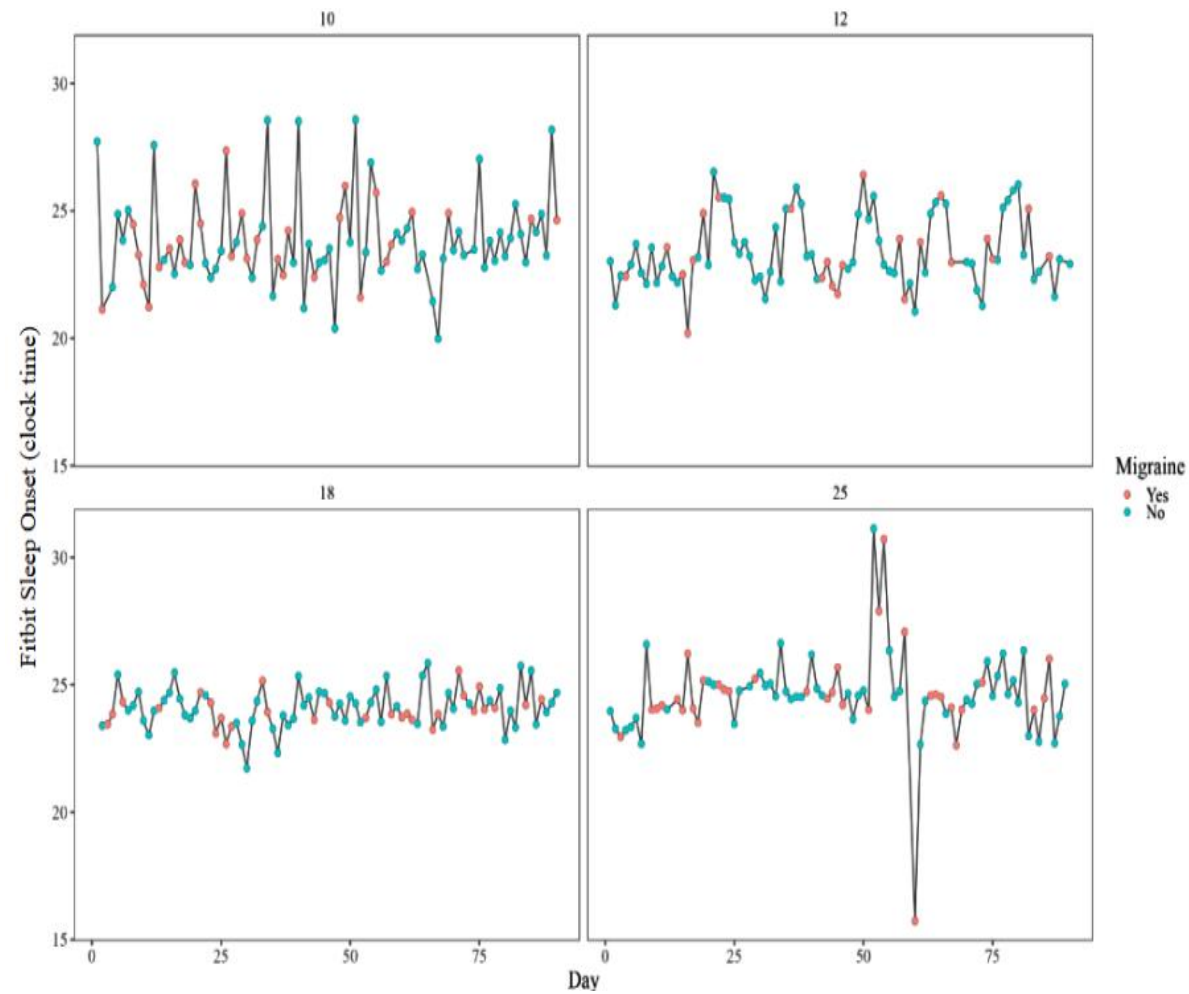


Figure H9. Line plots of Fitbit Sleep Onset time of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

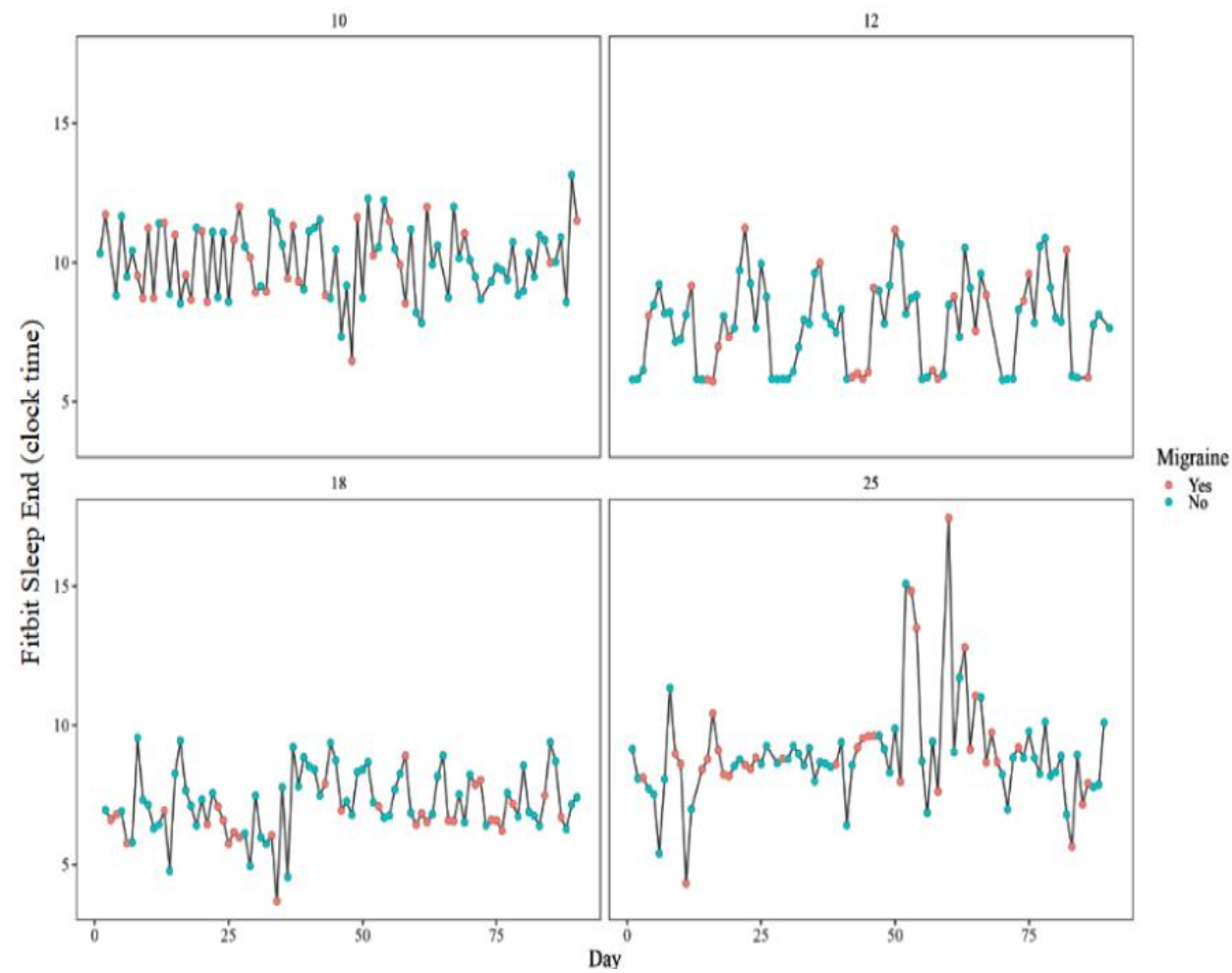


Figure H10. Line plots of Fitbit Sleep End of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

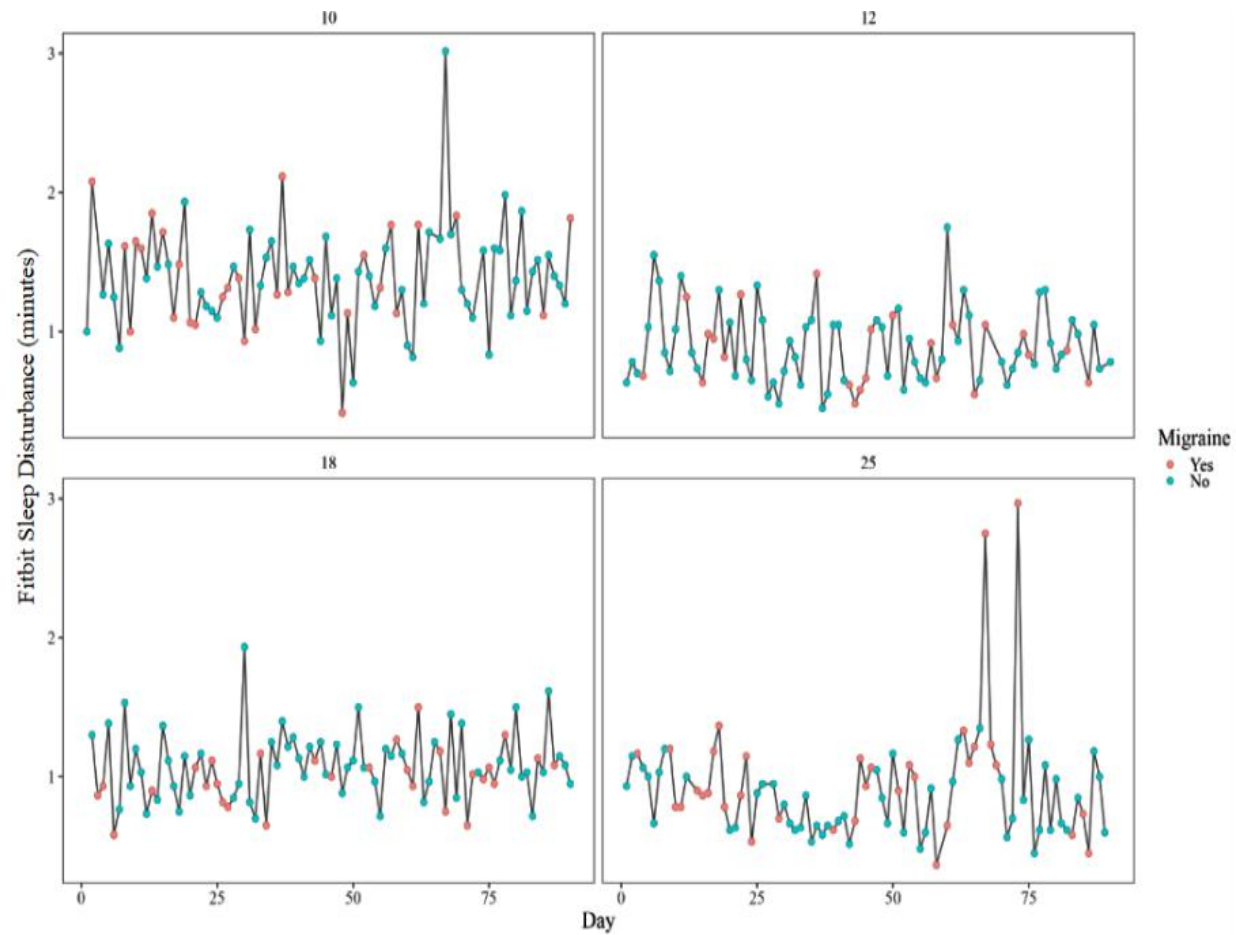


Figure H11. Line plots of Fitbit Sleep Disturbance (minutes) of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

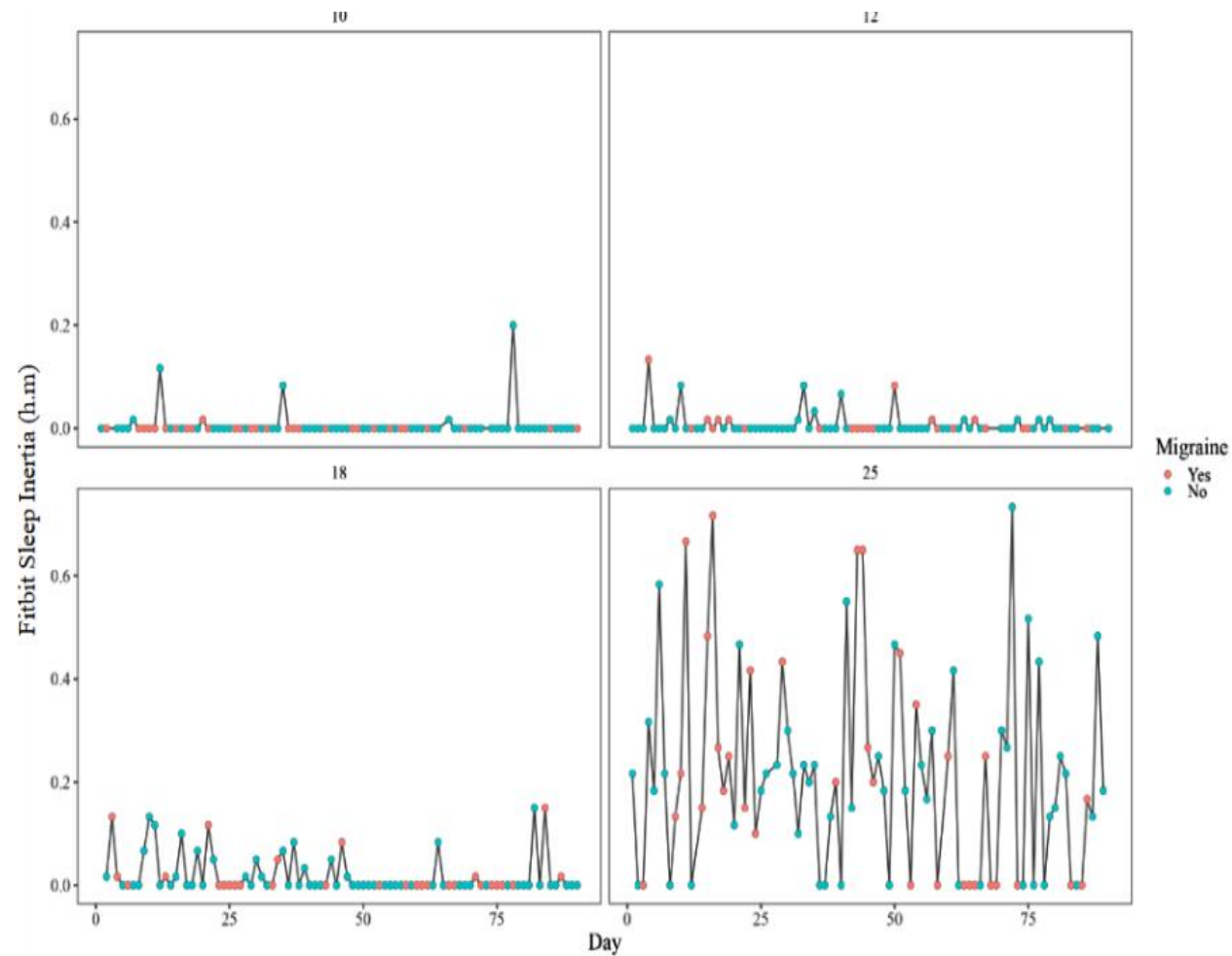


Figure H12. Line plots of Fitbit Sleep Inertia (h.m) four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

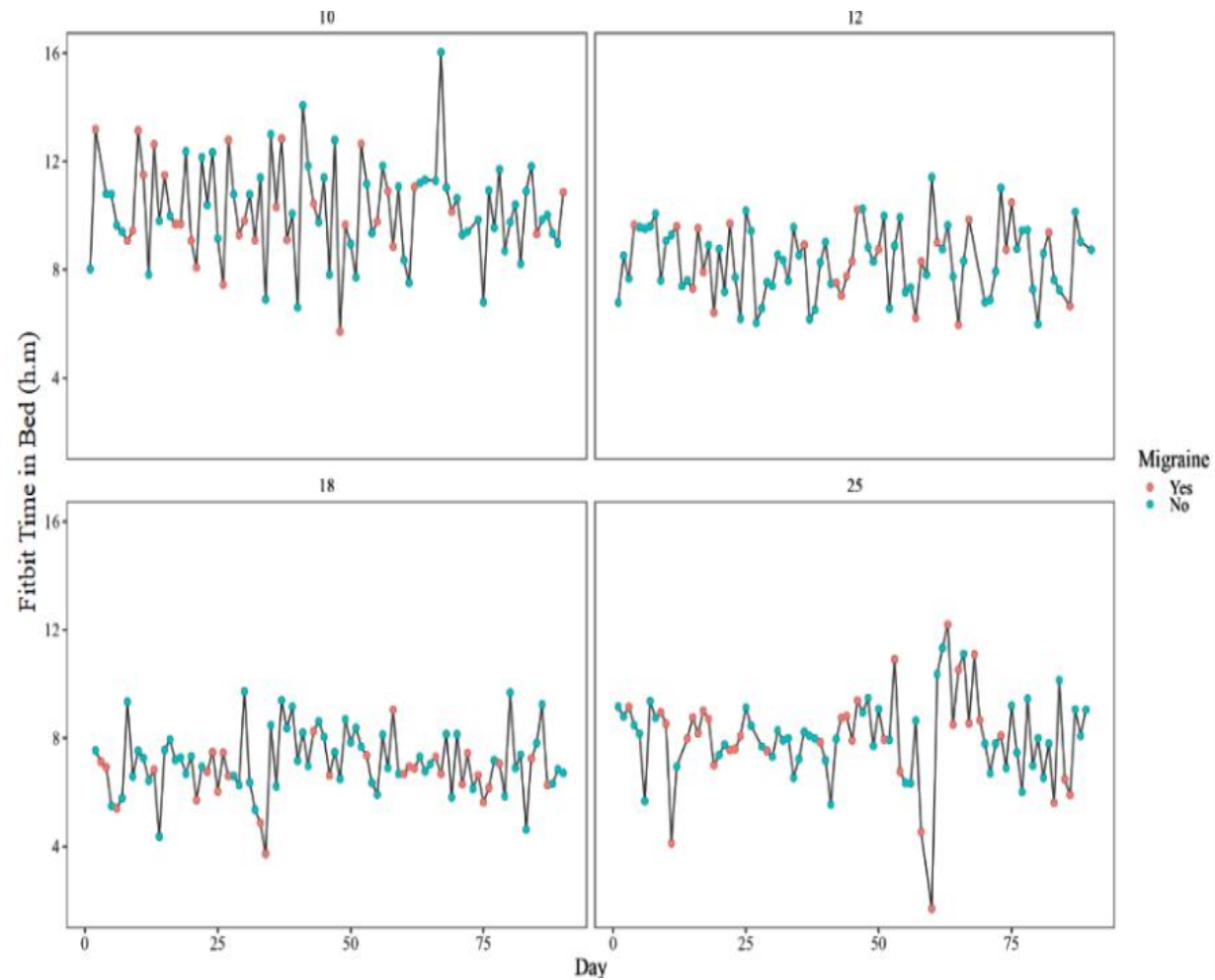


Figure H13. Line plots of Fitbit Time in Bed (h.m) of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

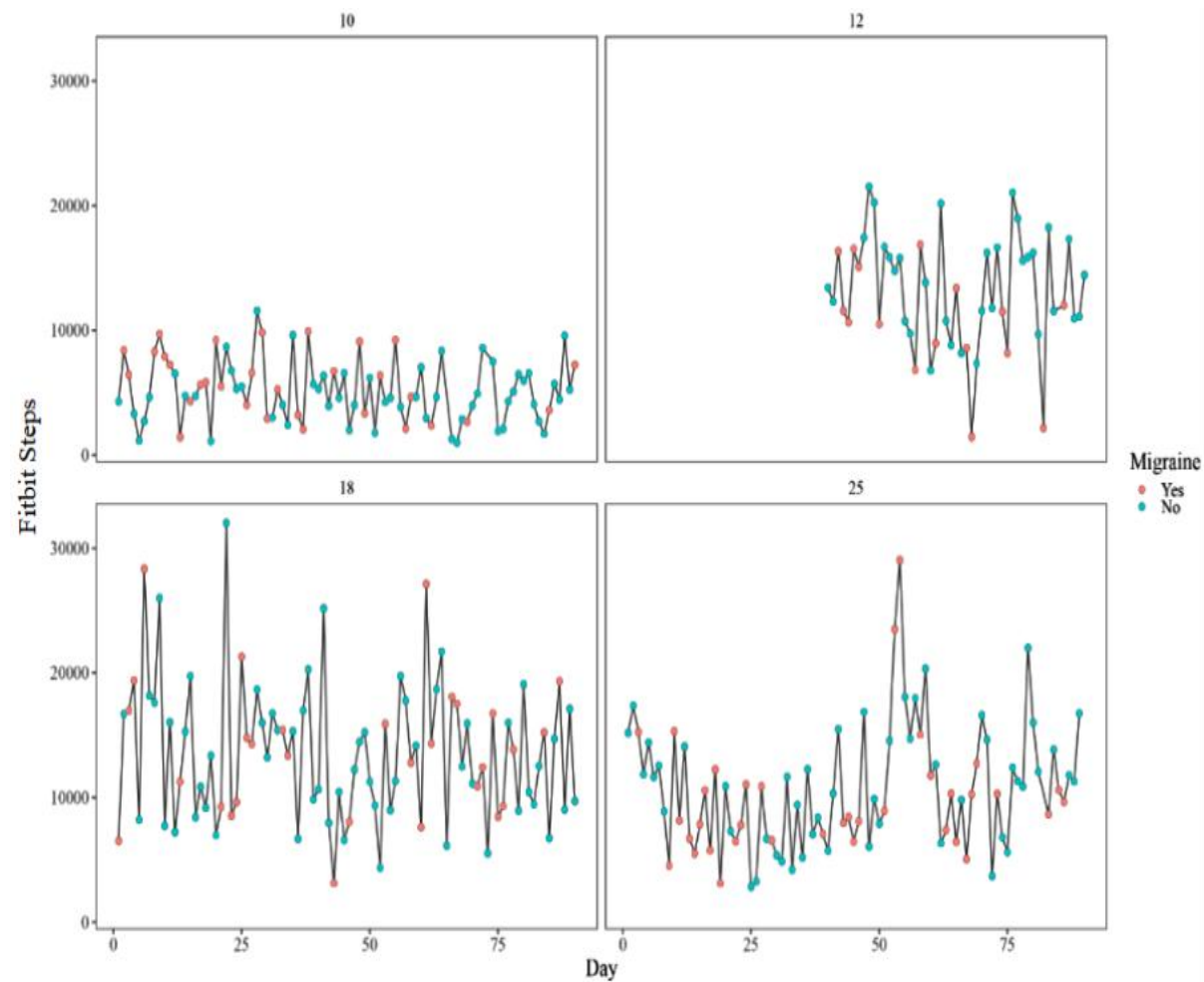


Figure H14. Line plots of Fitbit Step Count of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

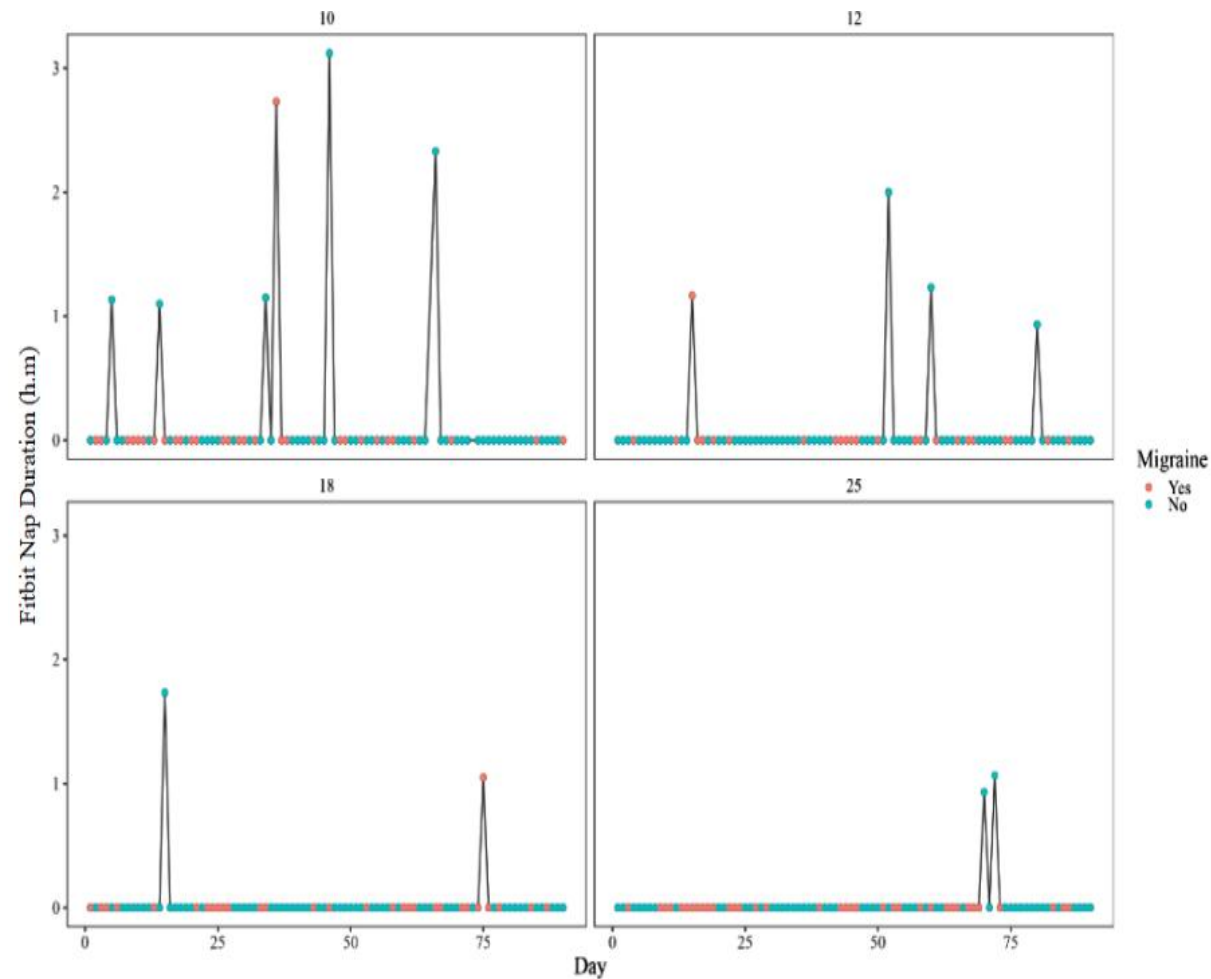


Figure H15. Line plots of Fitbit Nap Duration (h.m) of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

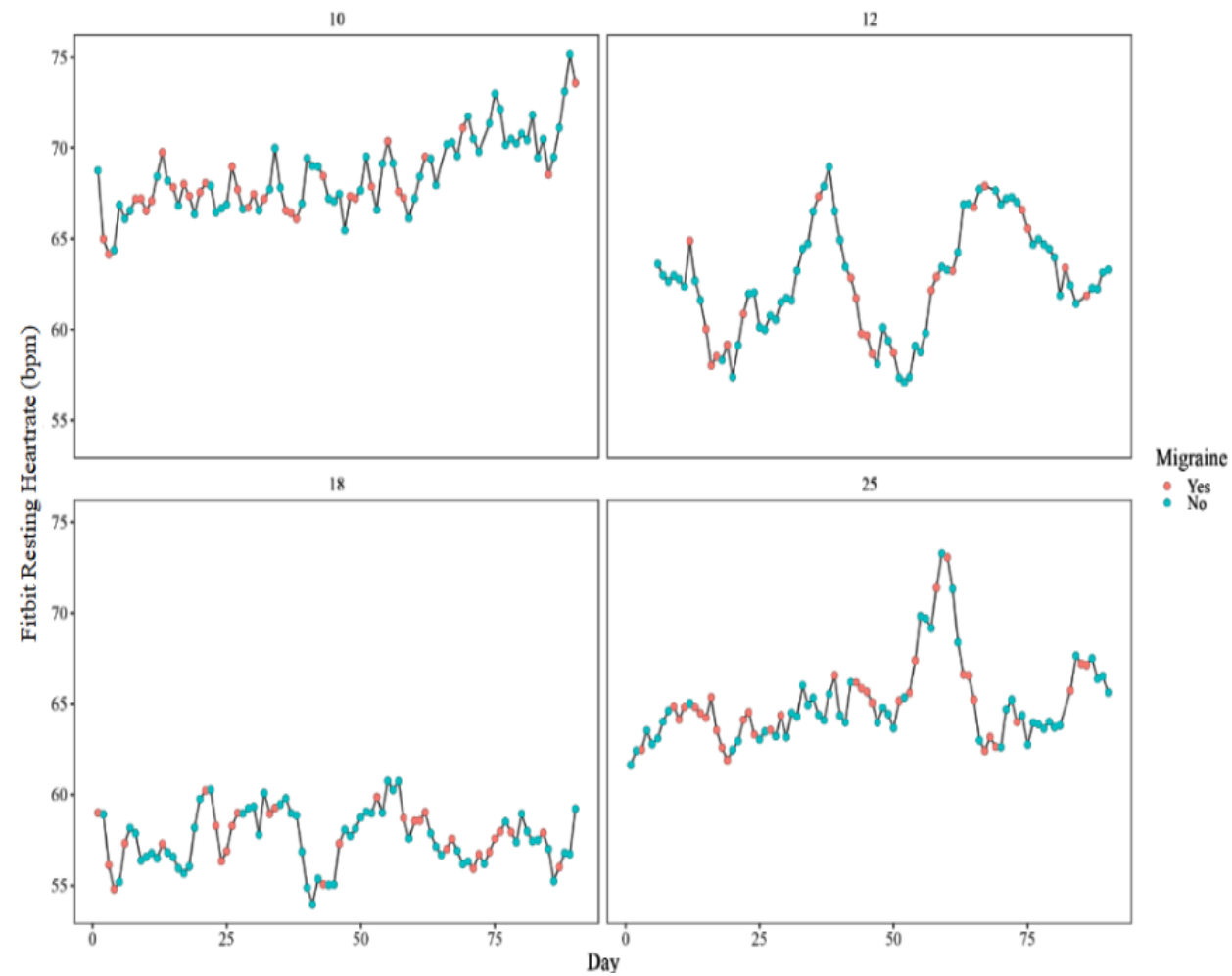


Figure H16. Line plots of Fitbit Resting Heartrate of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

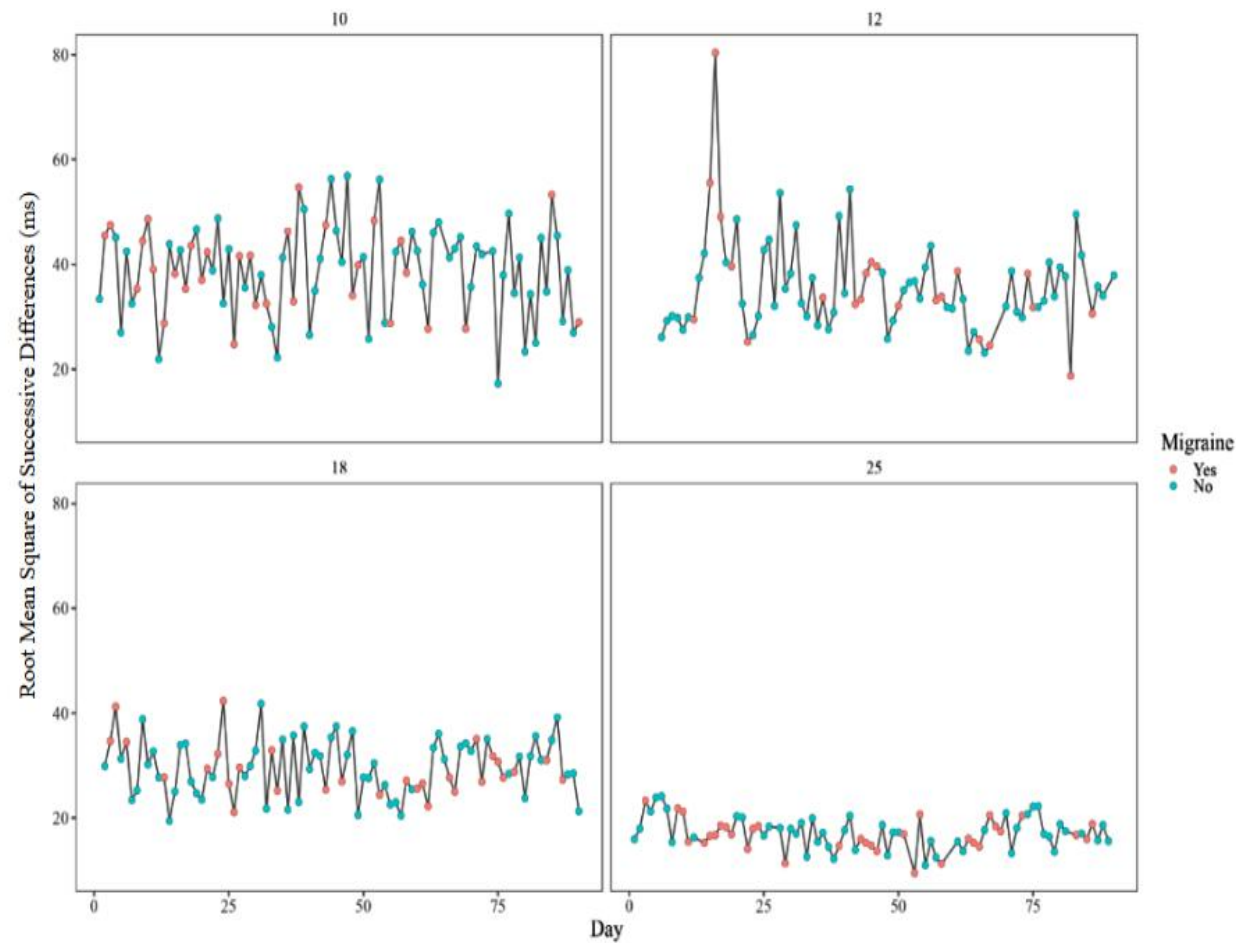


Figure H17. Line plots of Root Mean Square of Successive Differences of four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

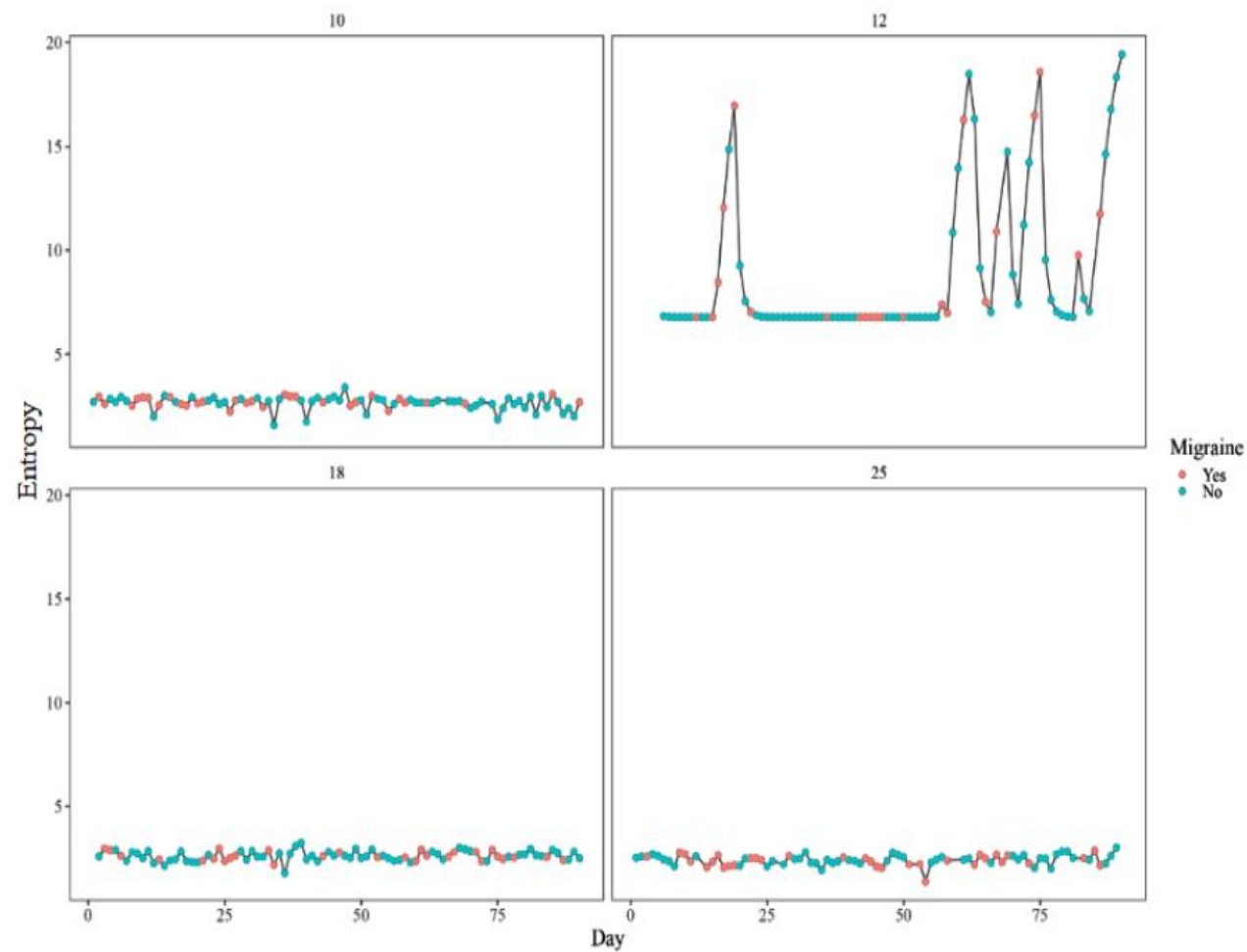


Figure H18. Line plots of daily entropy values from four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

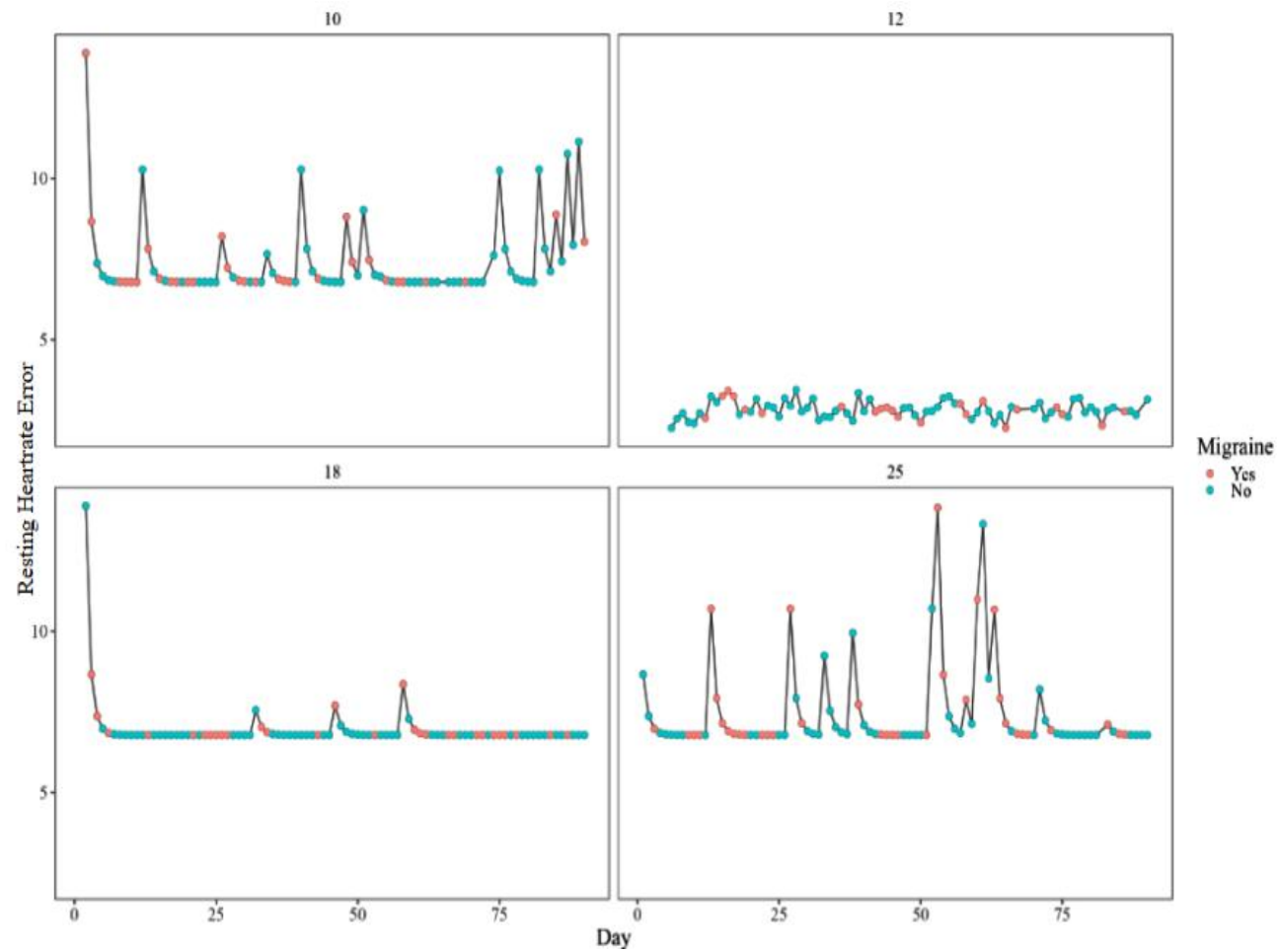


Figure H19. Line plots of daily Resting Heartrate Error from four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

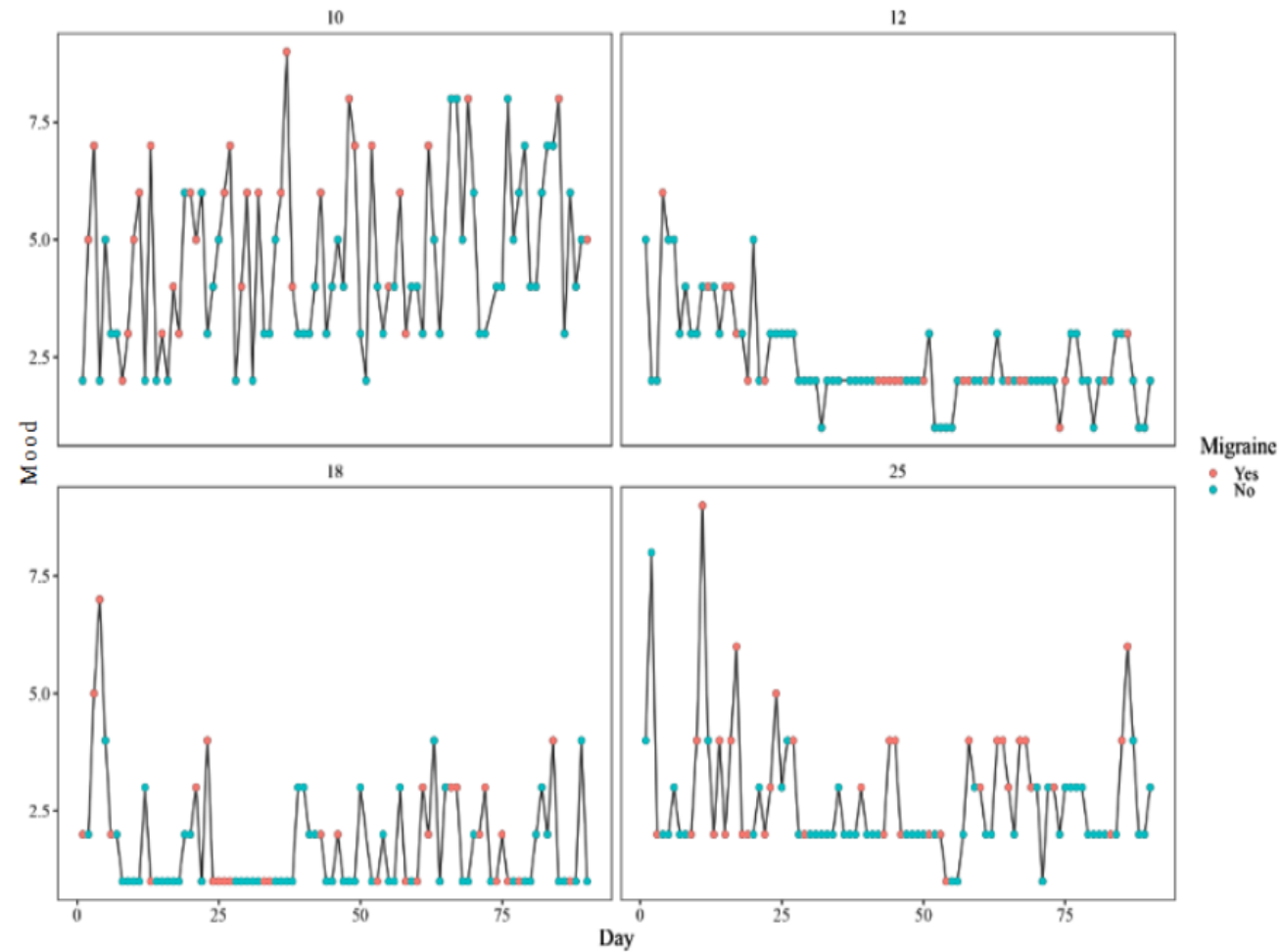


Figure H20. Line plots of daily self-reported Mood from four participants across the 90-day study period. Markers added at each daily score to distinguish migraine and non-migraine days. Red markers indicate a migraine and blue indicate no migraine.

Appendix I: Descriptive statistics of the neuropsychological tests per testing session from Section E, Chapter Five.

Table I1. Descriptive summary statistics of neuropsychological variables for each of the eight sessions. Sessions 1 and 8 were completed between migraine attacks and represent baseline and interictal functioning. Sessions 2, 4 and 6 were completed 24 hours after migraine pain had ended. Sessions 3, 5 and 7 were completed 48 hours after migraine pain had ended.

Session	Variable	N	Minimum	Maximum	Mean	Std. Error
1	Trail A Error	15	0	18	5.00	1.47
	Trail A Time (ms)	15	56917	294622	125501.53	15995.00
	Trail B Error	15	0	11	3.80	0.75
	Trail B Time (ms)	15	37554	152564	89633.67	10787.42
	Total Trail Error	15	0	25	9.27	1.92
	Total Trail Time (ms)	15	102909	470976	233603.07	26787.49
	BML	15	5	8	6.80	0.24
	BMS	15	4	8	6.17	0.29
	Go/ No-Go Time (ms)	15	771714	1495079	861169.60	49816.39
	Go/ No-Go Errors	15	0	1	0.09	0.06
	Omission Errors	15	0	1	0.10	0.06
	Commission Errors	15	0	1	0.08	0.06
2	Variable	N	Minimum	Maximum	Mean	Std. Error
	Trail A Error	12	0	2	0.50	0.23
	Trail A Time (ms)	12	24572	84986	50113.33	4968.13
	Trail B Error	12	0	3	1.25	0.35
	Trail B Time (ms)	12	35348	222419	74284.08	14657.77
	Total Trail Error	12	0	5	2.08	0.54
	Total Trail Time (ms)	12	80934	321763	139007.67	19650.33
	BML	12	3	9	6.92	0.48
	BMS	12	3	9	6.62	0.43
	Go/ No-Go Time (ms)	11	756577	810408	782972.45	5323.23
	Go/ No-Go Errors	11	0	0	0.01	0.00
	Omission Errors	11	0	0	0.01	0.01

	Commission Errors	11	0	0	0.01	0.00
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3	Variable	N	Minimum	Maximum	Mean	Std. Error
	Trail A Error	10	0	7	2.70	0.86
	Trail A Time (ms)	10	59681	162628	90704.90	10613.87
	Trail B Error	10	0	5	2.10	0.61
	Trail B Time (ms)	10	48644	132602	85177.70	9249.02
	Total Trail Error	10	1	12	5.00	1.27
	Total Trail Time (ms)	10	121846	301124	187930.90	20450.39
	BML	10	6	9	7.40	0.37
	BMS	10	6	9	6.94	0.33
	Go/ No-Go Time (ms)	10	753624	810304	780904.10	5888.90
	Go/ No-Go Errors	10	0	1	0.23	0.13
	Omission Errors	10	0	1	0.24	0.13
	Commission Errors	10	0	1	0.21	0.13

4	Variable	N	Minimum	Maximum	Mean	Std. Error
	Trail A Error	10	0	5	2.40	0.45
	Trail A Time (ms)	10	55009	152285	97114.00	11014.59
	Trail B Error	10	0	4	1.20	0.39
	Trail B Time (ms)	10	40233	119864	76821.20	8122.77
	Total Trail Error	10	1	6	3.70	0.42
	Total Trail Time (ms)	10	106780	278162	184670.60	18704.08
	BML	10	6	11	7.80	0.47
	BMS	10	5	10	7.07	0.54
	Go/ No-Go Time (ms)	10	756619	800768	778709.30	4763.85
	Go/ No-Go Errors	10	0	1	0.12	0.10
	Omission Errors	10	0	1	0.14	0.10
	Commission Errors	10	0	1	0.11	0.10

5	Variable	N	Minimum	Maximum	Mean	Std. Error
	Trail A Error	9	1	8	2.33	0.75
	Trail A Time (ms)	9	58878	296499	134706.56	25946.44
	Trail B Error	9	1	5	2.11	0.42
	Trail B Time (ms)	9	46946	178963	87516.67	13440.44

	Total Trail Error	9	2	10	4.78	0.85
	Total Trail Time (ms)	9	111666	430860	232967.44	38315.32
	BML	9	7	11	8.78	0.52
	BMS	9	6	10	8.29	0.41
	Go/ No-Go Time (ms)	9	764154	1286368	835384.44	56510.49
	Go/ No-Go Errors	9	0	0	0.02	0.01
	Omission Errors	9	0	0	0.03	0.02
	Commission Errors	9	0	0	0.01	0.00
6	Variable	N	Minimum	Maximum	Mean	Std. Error
	Trail A Error	8	0	5	1.75	0.62
	Trail A Time (ms)	8	68489	151836	106758.00	11495.05
	Trail B Error	8	0	20	6.50	2.63
	Trail B Time (ms)	8	43348	1097696	231461.00	124641.48
	Total Trail Error	8	0	23	8.63	3.06
	Total Trail Time (ms)	8	116645	1267065	353206.00	132281.07
	BML	8	6	9	7.75	0.41
	BMS	8	5	8	7.16	0.43
	Go/ No-Go Time (ms)	0	0	0	0	0
	Go/ No-Go Errors	0	0	0	0	0
	Omission Errors	0	0	0	0	0
	Commission Errors	0	0	0	0	0
7	Variable	N	Minimum	Maximum	Mean	Std. Error
	Trail A Error	8	1	3	1.88	0.30
	Trail A Time (ms)	8	51149	221911	117370.63	22845.53
	Trail B Error	8	0	6	1.38	0.68
	Trail B Time (ms)	8	48648	190096	89048.63	16256.82
	Total Trail Error	8	1	9	3.75	0.88
	Total Trail Time (ms)	8	107139	416900	218229.00	38629.52
	BML	8	7	11	8.38	0.57
	BMS	8	6	10	7.91	0.53
	Go/ No-Go Time (ms)	8	761187	787360	773936.25	3203.23
	Go/ No-Go Errors	8	0	0	0.01	0.01
	Omission Errors	8	0	0	0.02	0.01

Commission Errors	8	0	0	0.01	0.00
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8	Variable	N	Minimum	Maximum	Mean	Std. Error
	Trail A Error	11	1	6	2.55	0.53
	Trail A Time (ms)	11	47016	175846	100521.27	11307.83
	Trail B Error	11	0	5	2.55	0.56
	Trail B Time (ms)	11	30701	120398	59800.91	8603.19
	Total Trail Error	11	2	11	5.18	0.84
	Total Trail Time (ms)	11	82017	310495	171023.00	19784.62
	BML	13	5	9	6.77	0.36
	BMS	13	4	9	6.23	0.38
	Go/ No-Go Time (ms)	13	757575	830514	785844.46	6382.04
	Go/ No-Go Errors	13	0	1	0.14	0.08
	Omission Errors	13	0	1	0.19	0.10
	Commission Errors	13	0	1	0.09	0.08

Appendix J: Neuropsychological Test Materials used in Chapter Five.

J.1 Baseline One / Session One:

Go / No-Go Test

Vertical Go



Horizontal Go



Vertical No-Go



Horizontal No-Go



Trail Making Test

Trail Making Test – Trail A

Trail 1

Time in Seconds: _____

Start
1

End
25

CTMT

Page 5

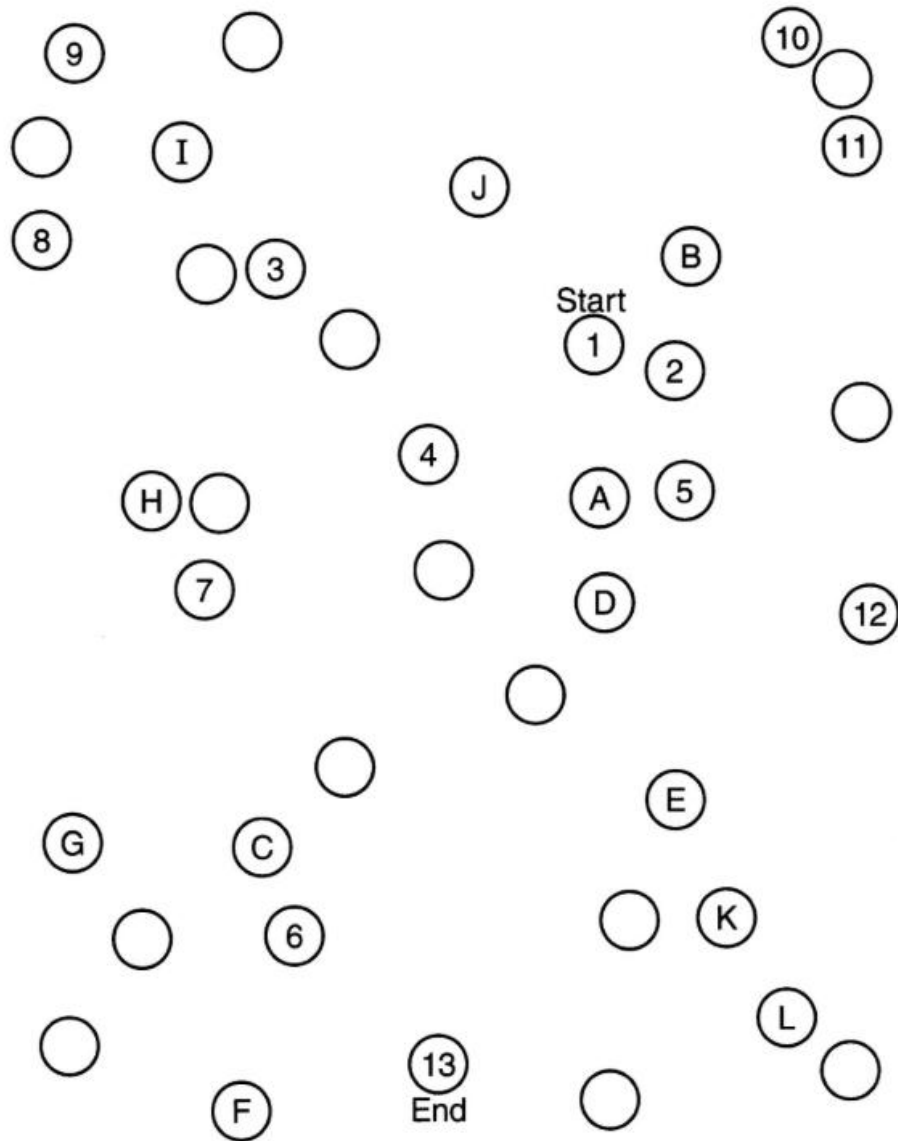
Diagram illustrating the Trail Making Test (Trail A) setup. The test consists of 25 numbered circles arranged in a non-sequential pattern. The sequence starts at circle 1 (labeled "Start") and ends at circle 25 (labeled "End"). The circles are numbered 1 through 25, with the numbers scattered across the page. The sequence is: 1 (Start), 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 (End).

Trail Making Test

Trail Making Test – Trail B

Trail 5

Time in Seconds: _____



CTMT

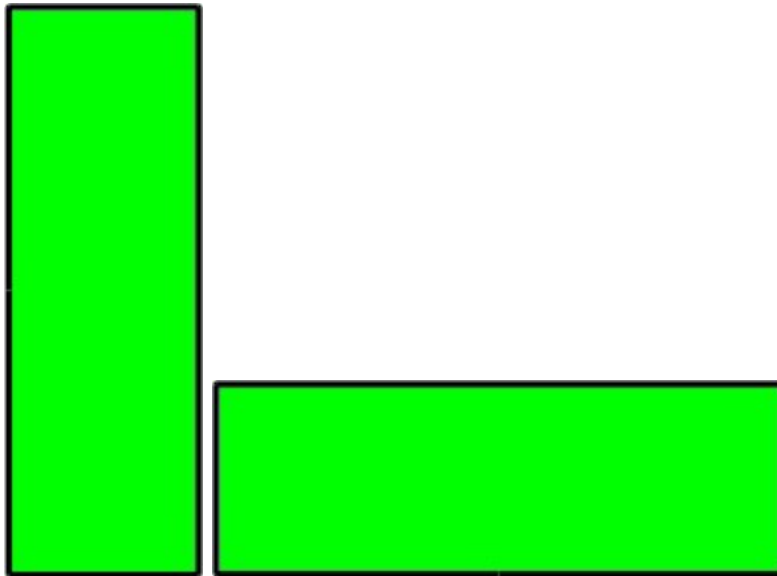
Page 17

J.2. 24-hours after Migraine One / Session 3

Go / No-Go Test

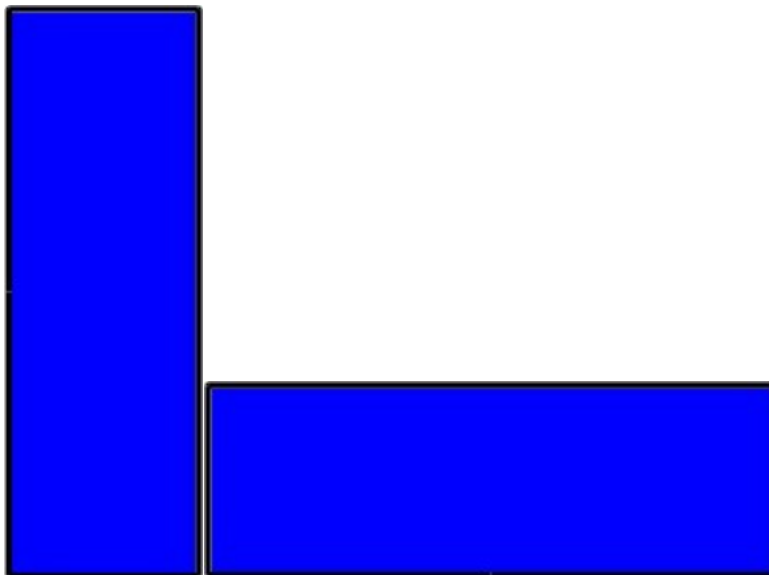
Vertical Go

Horizontal Go



Vertical No-Go

Horizontal No-Go



Trail Making Test

Trail Making Test – Trail A

Trail 1

Time in Seconds: _____

The diagram shows 25 numbered circles arranged in a non-linear fashion. The path starts at circle 1, labeled 'Start'. The path proceeds to circle 2, then 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, and finally to circle 25, labeled 'End'. The path is a continuous line connecting the circles in numerical order.

CTMT

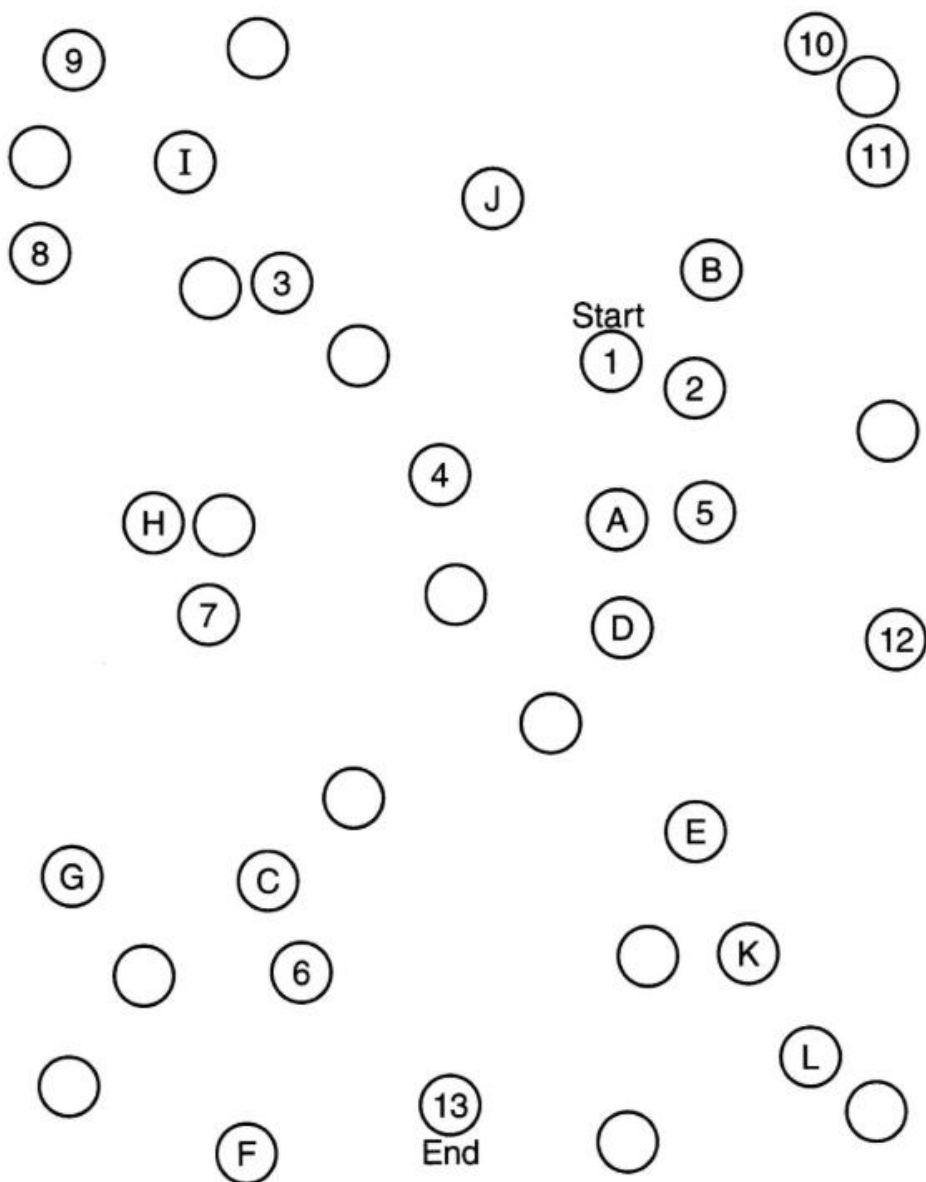
Page 5

Trail Making Test

Trail Making Test – Trail B

Trail 5

Time in Seconds: _____



CTMT

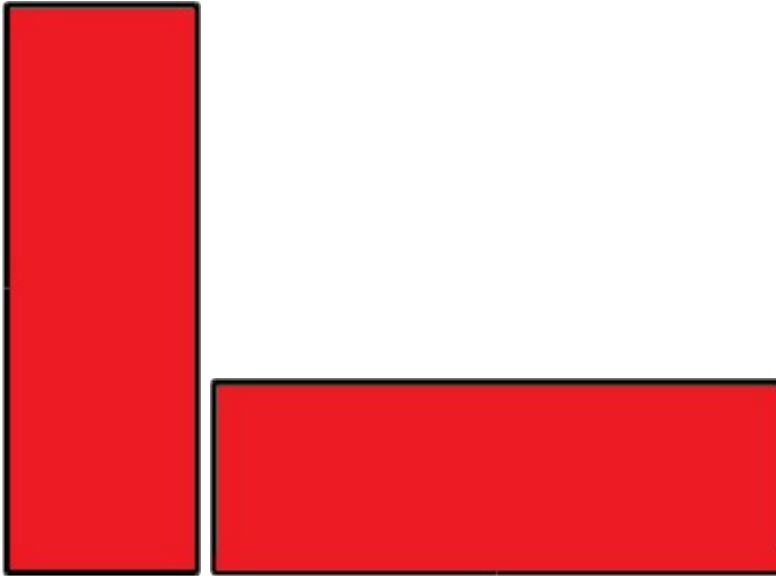
Page 17

J.3. 48-hours after Migraine One – Session 3

Go / No-Go Test

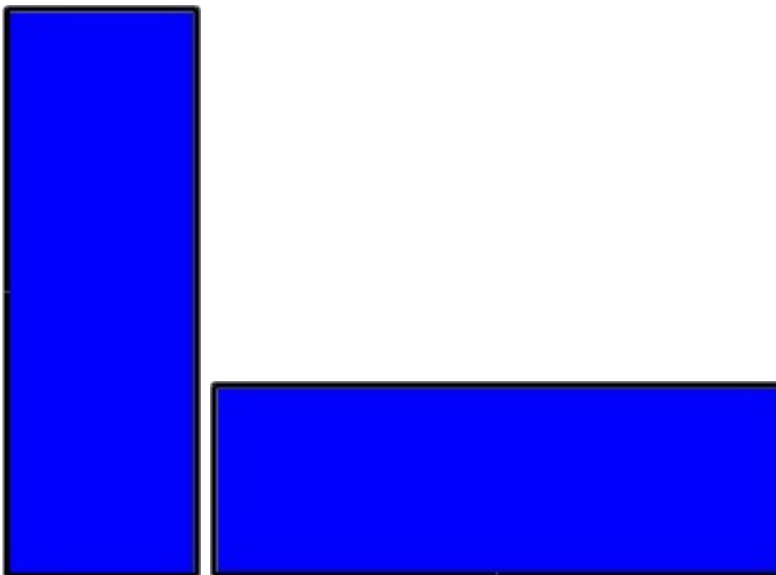
Vertical Go

Horizontal Go



Vertical No-Go

Horizontal No-Go



Trail Making Test

Trail Making Test- Trail A

Trail 1

Time in Seconds: _____

The diagram shows 25 numbered circles (1-25) scattered on a page. A sequence of numbers is provided for the test: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25. The sequence starts at circle 1, which is labeled 'Start'. The sequence ends at circle 25, which is labeled 'End'. The circles are arranged in a way that requires the participant to connect them in the correct order to complete the trail.

Start
1

End
25

CTMT

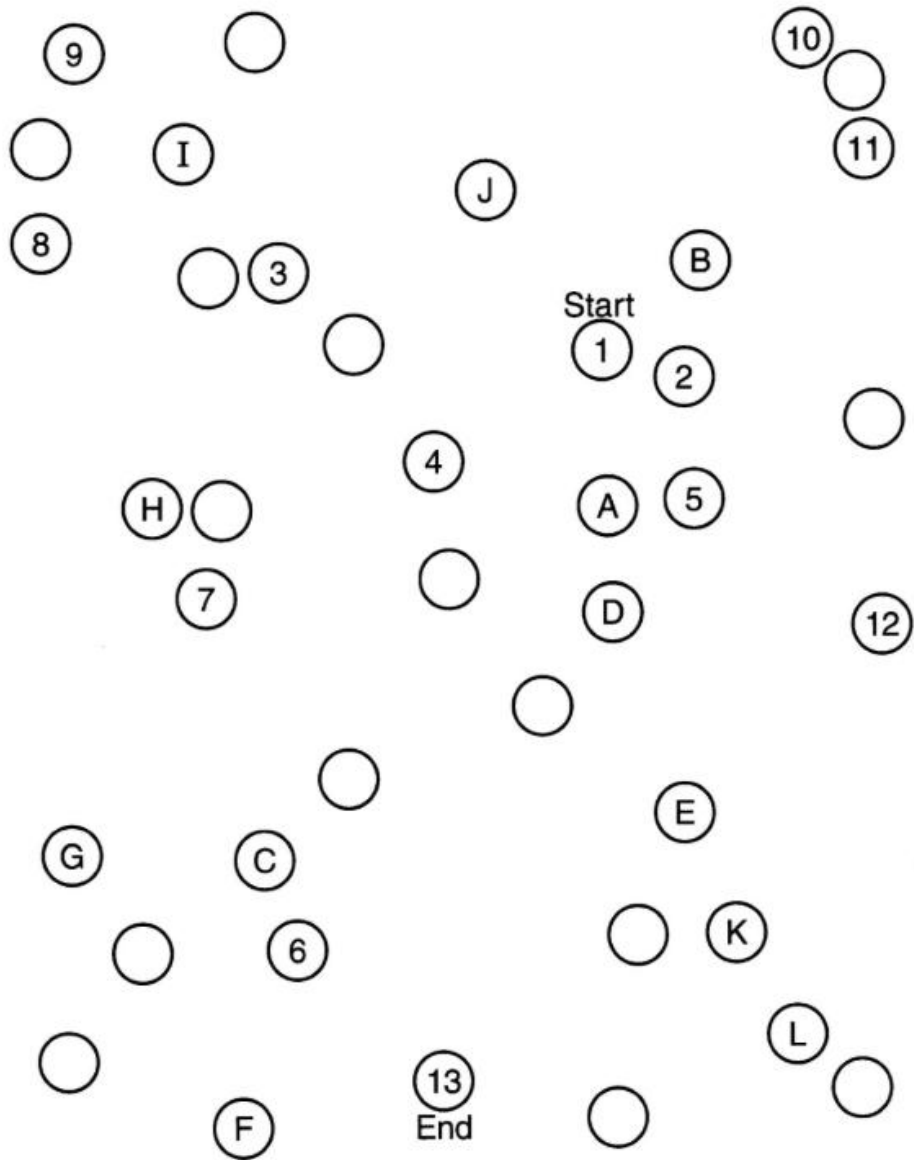
Page 5

Trail Making Test

Trail Making Test – Trail B

Trail 5

Time in Seconds: _____



CTMT

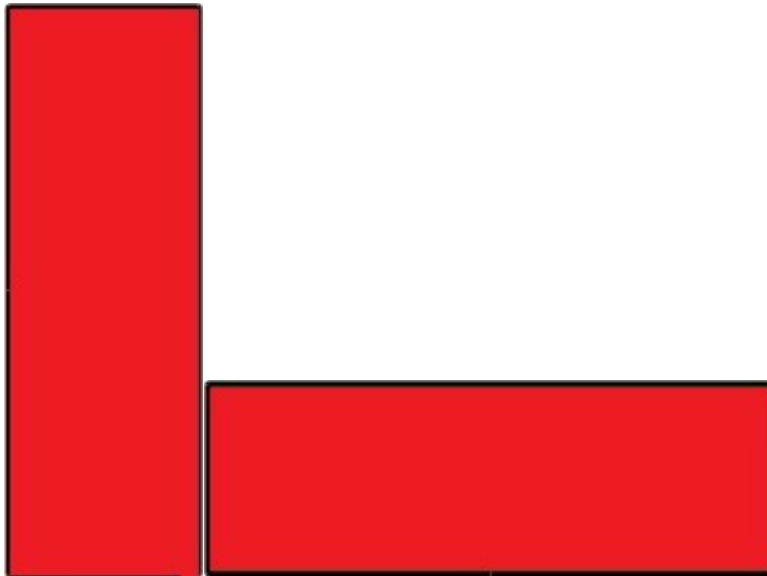
Page 17

J.4. 24-hours after Migraine 2 – Session 4

Go / No-Go Test

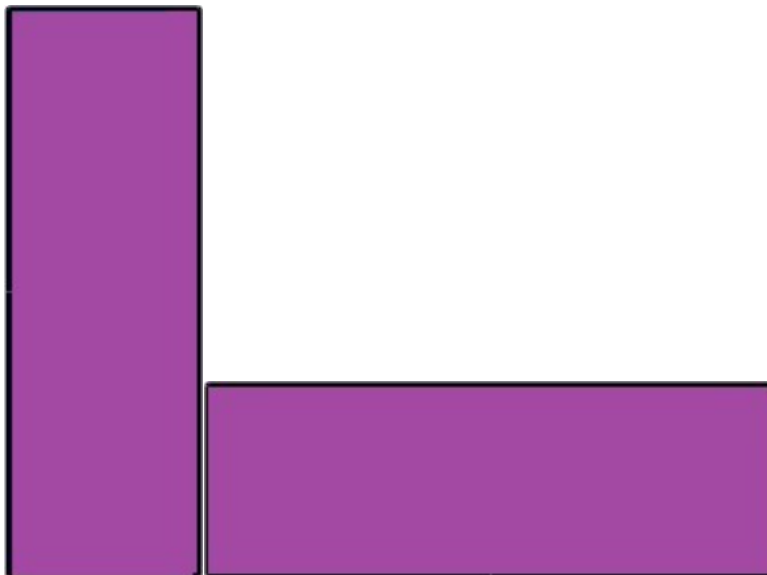
Vertical Go

Horizontal Go



Vertical No-Go

Horizontal No-Go



Trail Making Test

Trail Making Test – Trail A

Trail 1

Time in Seconds: _____

Start

End

CTMT

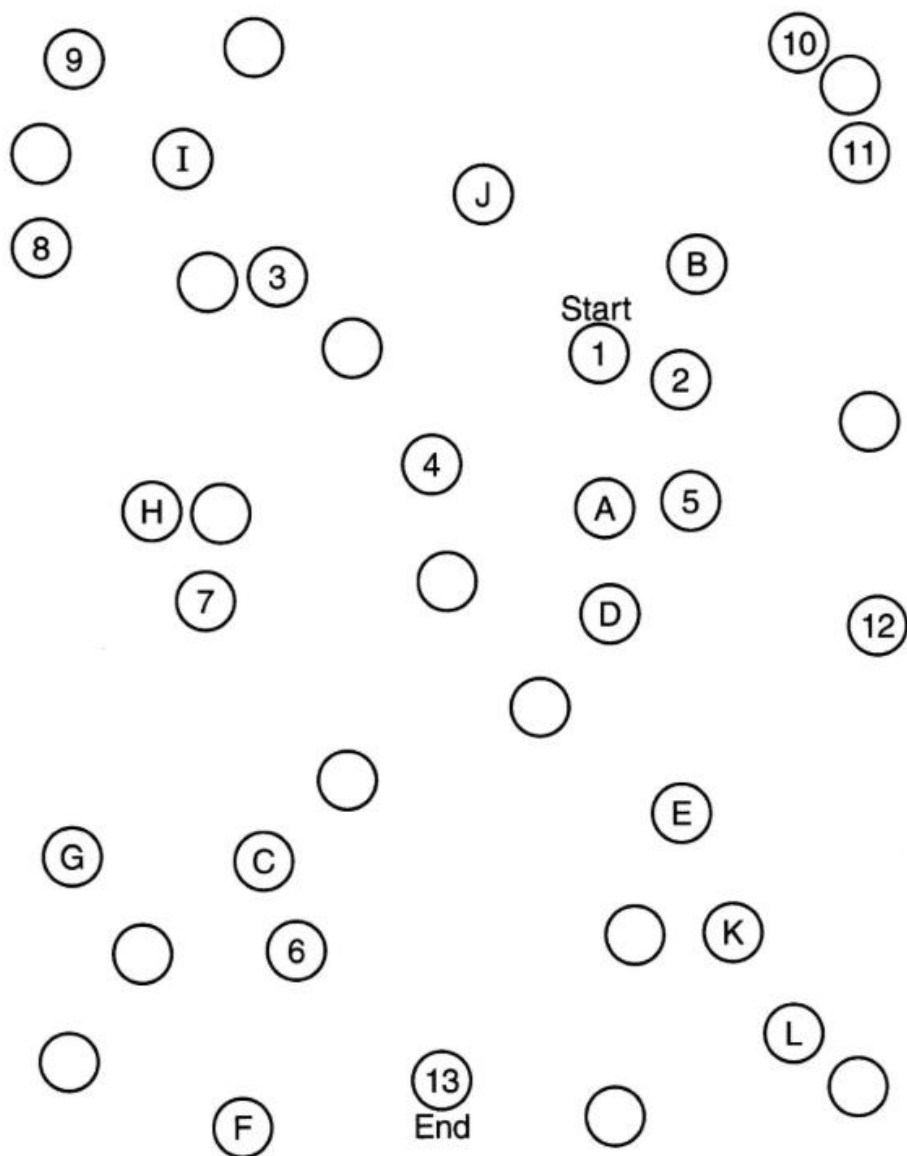
Page 5

Trail Making Test

Trail Making Test – Trail B

Trail 5

Time in Seconds: _____



CTMT

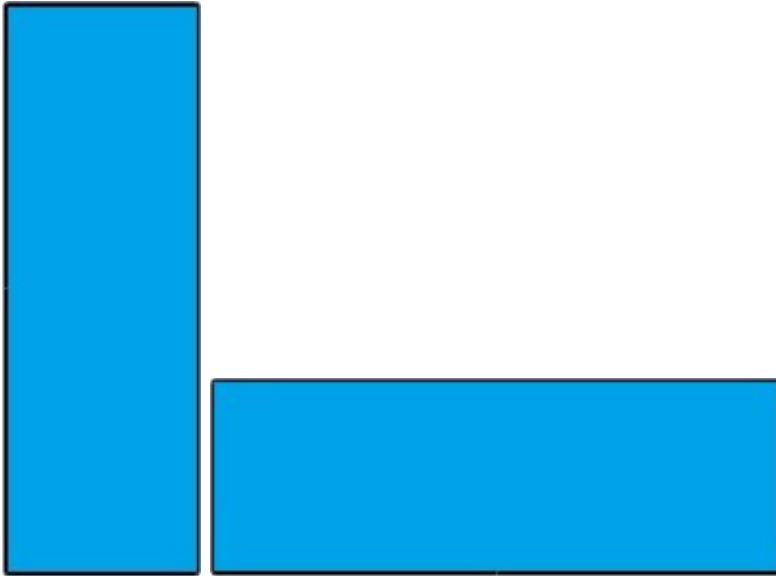
Page 17

J.5. 48-hours after Migraine 2 / Session 5

Go / No-Go Test

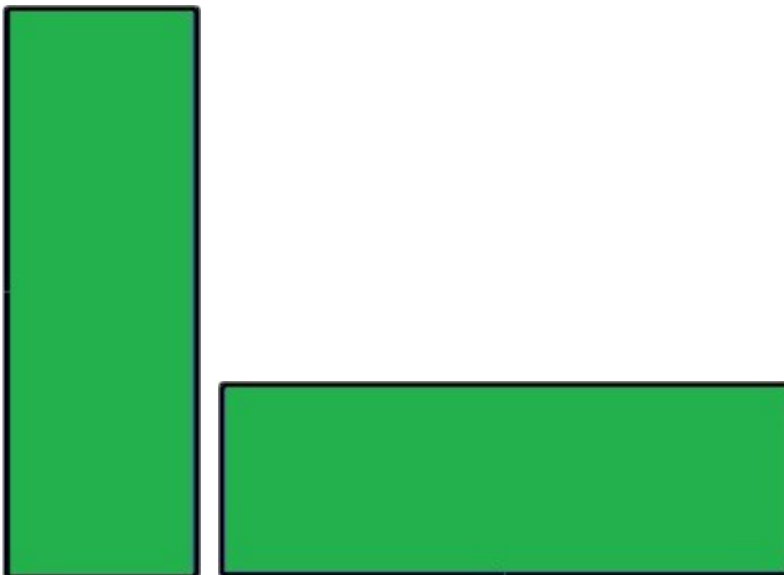
Vertical Go

Horizontal Go



Vertical No-Go

Horizontal No-Go



Trail Making Test

Trail Making Test – Trail A

Trail 1

Time in Seconds: _____

Start
1

End
25

CTMT

Page 5

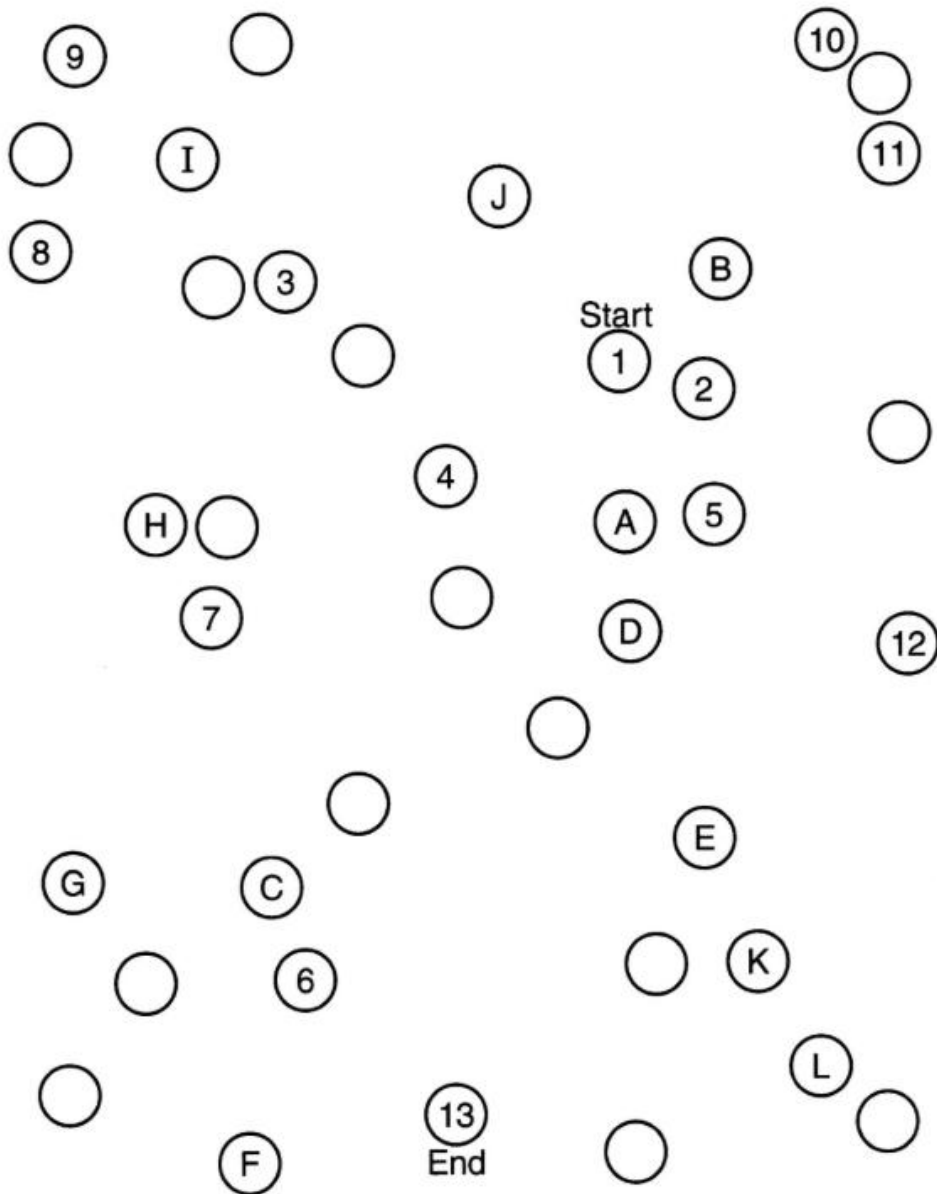
Diagram illustrating the Trail Making Test (Trail A) setup. The test consists of 25 numbered circles arranged in a non-sequential pattern. The sequence starts at circle 1 and ends at circle 25. The circles are distributed across the page, with some numbers appearing in pairs (e.g., 2 and 7, 4 and 12). The path is a single continuous line connecting the circles in numerical order.

Trail Making Test

Trail Making Test – Trail B

Trail 5

Time in Seconds: _____

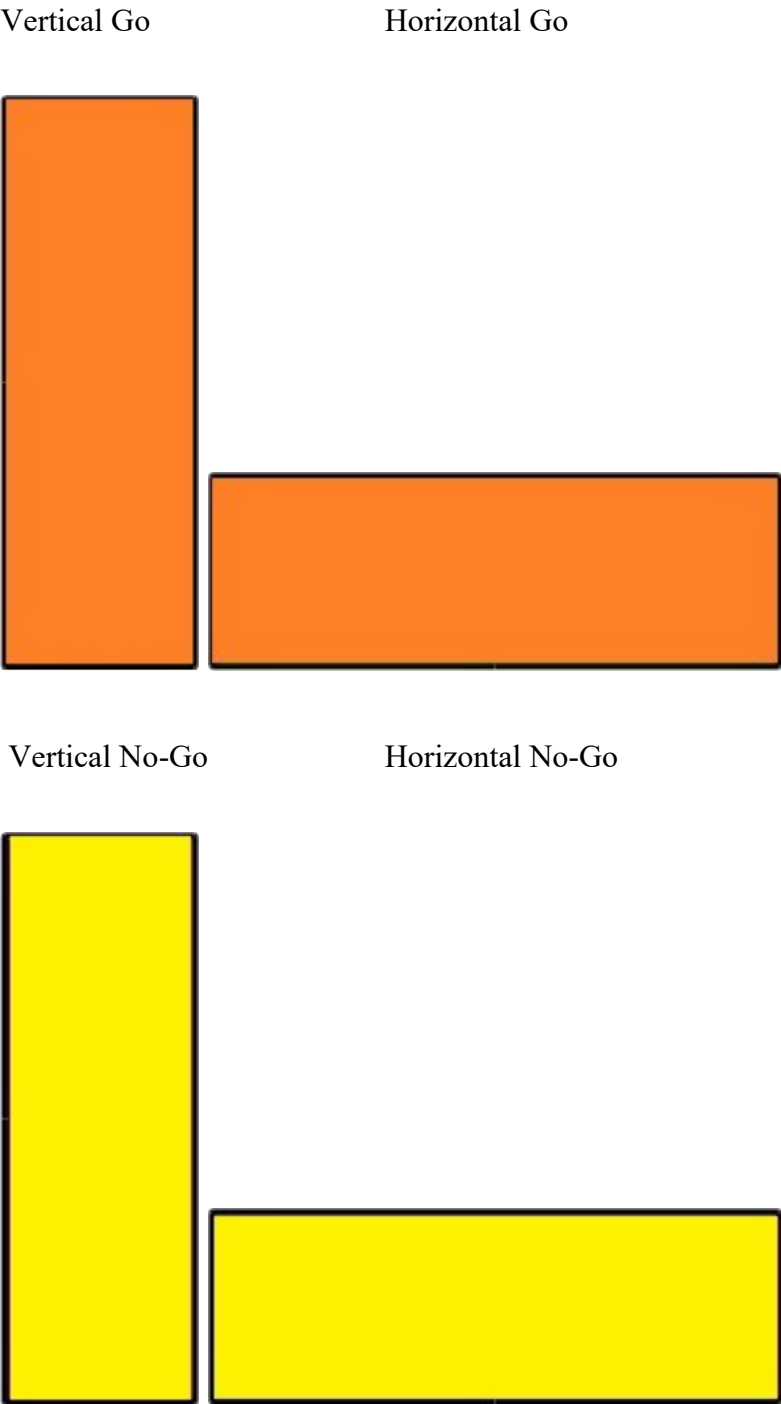


CTMT

Page 17

J.6. 48 hours after Migraine 3 – Session 7

Go / No-Go Test



Trail Making Test

Trail Making Test – Trail A

Trail 1

Time in Seconds: _____

The diagram shows 25 numbered circles (1-25) scattered on a page. A sequence of numbers is provided for the test: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25. The circles are arranged as follows: 1 (Start) is in the center; 2 and 7 are to its left; 3 is below it; 4 is to its right; 5 is below 4; 6 is at the bottom left; 8 is to the left of 6; 9 is at the top left; 10 is to the left of 2; 11 is to the right of 2; 12 is to the right of 4; 13 is to the right of 19; 14 is to the left of 11; 15 is at the top left; 16 is at the top right; 17 is to the right of 15; 18 is to the right of 14; 19 is to the right of 18; 20 is to the right of 16; 21 is at the bottom right; 22 is to the right of 12; 23 is to the right of 5; 24 is at the bottom center; 25 (End) is at the bottom right.

Start
1

End
25

CTMT

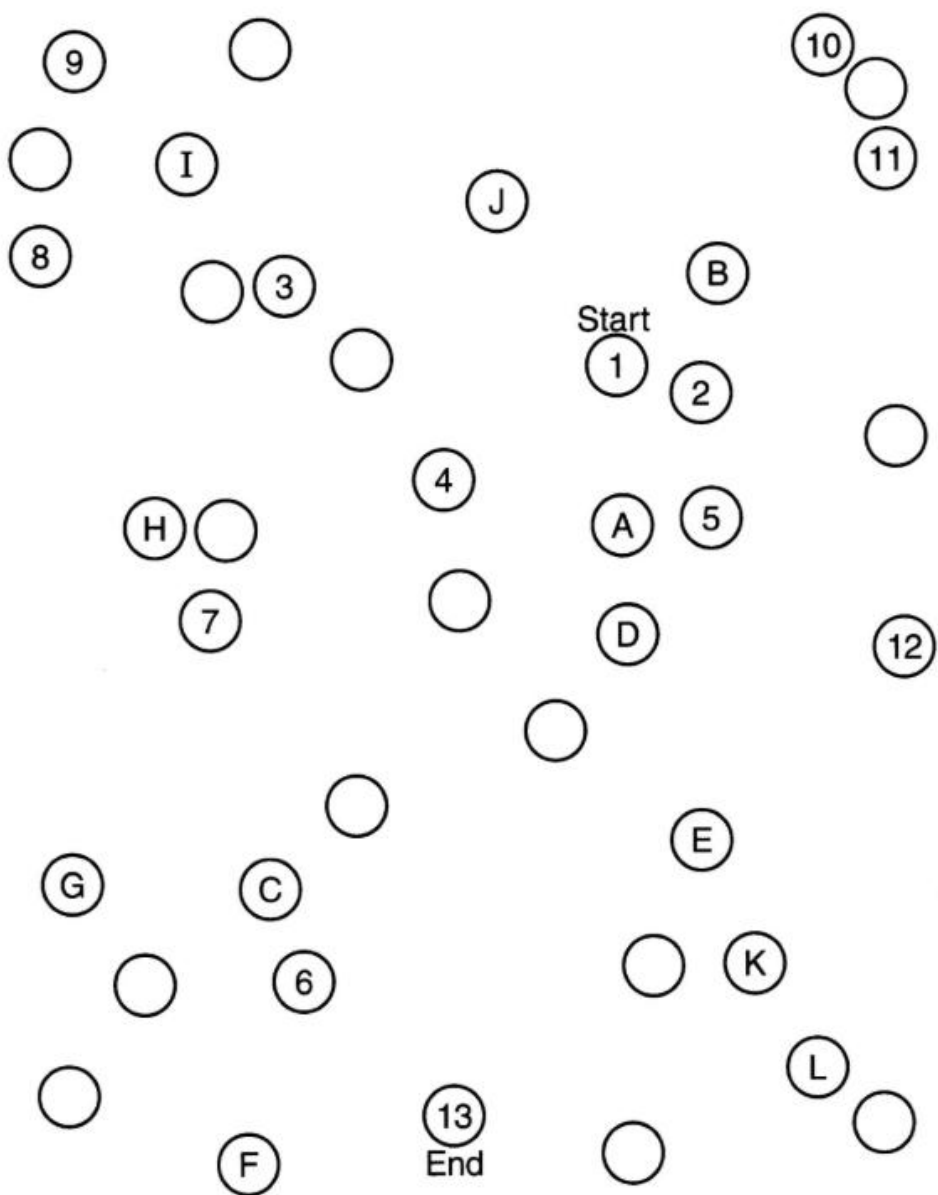
Page 5

Trail Making Test

Trail Making Test – Trail B

Trail 5

Time in Seconds: _____



CTMT

Page 17

J.7. Baseline 2 – Session 8

Go / No-Go Test

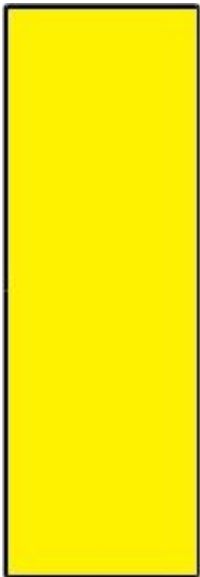
Vertical Go



Horizontal Go



Vertical No-Go



Horizontal No-Go

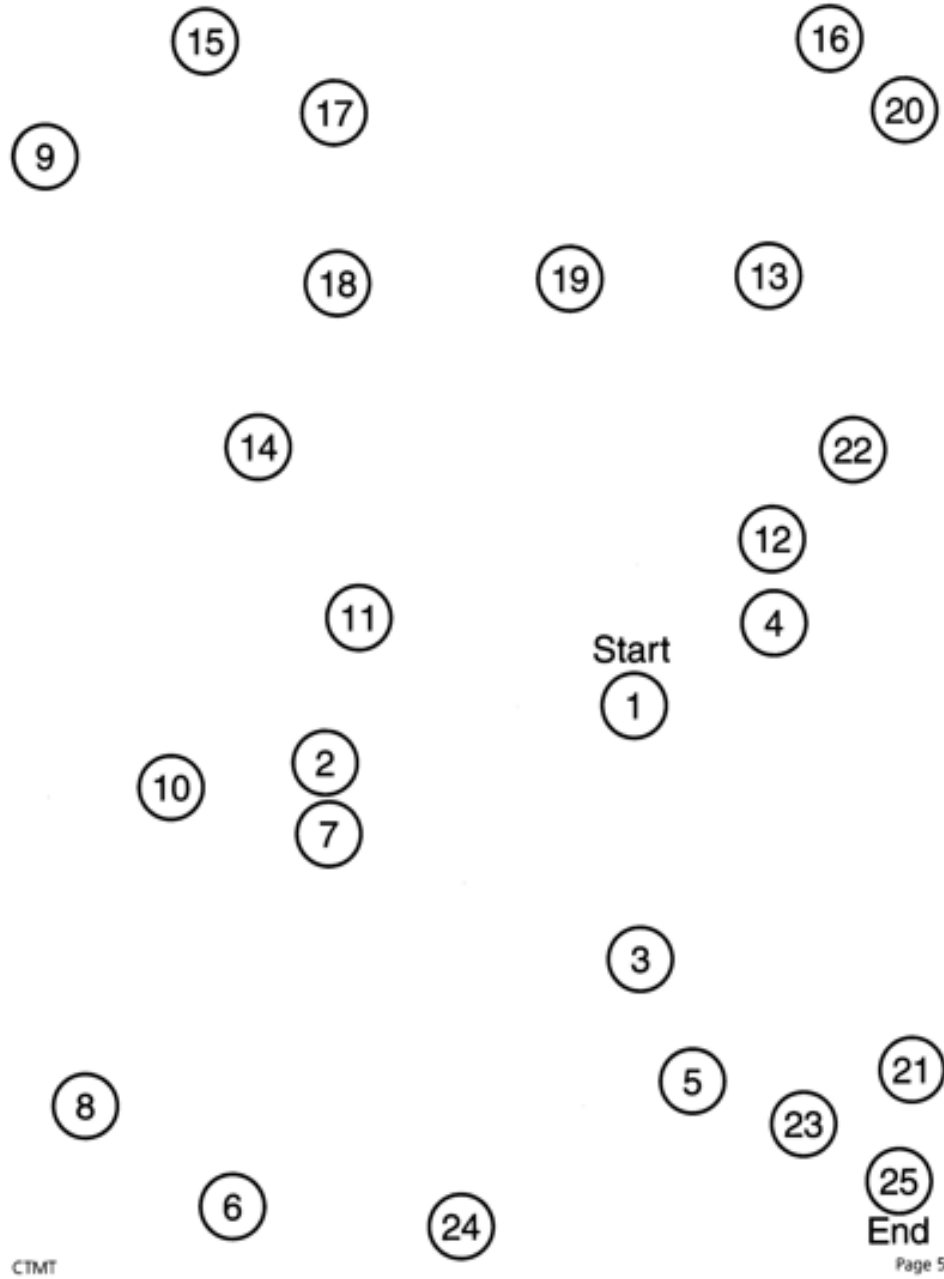


Trail Making Test

Trail Making Test – Trail A

Trail 1

Time in Seconds: _____



CTMT

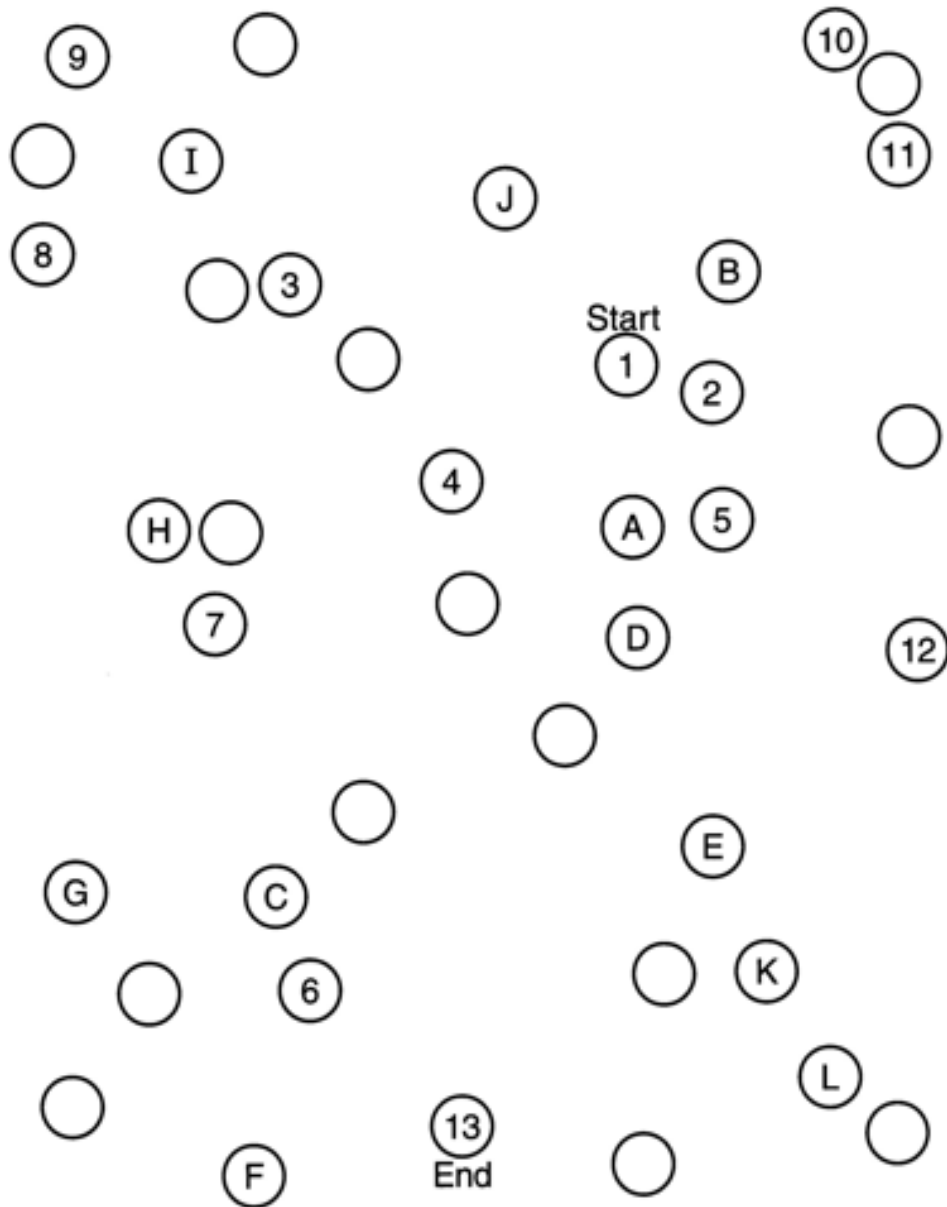
Page 5

Trail Making Test

Trail Making Test – Trail B

Trail 5

Time in Seconds: _____



CTMT

Page 17