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Virtual Morris water maze: opportunities and challenges

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Abstract: The ability to accurately recall locations and navigate our environment relies on multiple cognitive mechanisms. The behavioural and neural correlates of spatial navigation have been repeatedly examined using different types of mazes and tasks with animals. Accurate performances of many of these tasks have proven to depend on specific circuits and brain structures and some have become the standard test of memory in many disease models. With the introduction of virtual reality (VR) to neuroscience research, VR tasks have become a popular method of examining human spatial memory and navigation. However, the types of VR tasks used to examine navigation across laboratories appears to greatly differ, from open arena mazes and virtual towns to driving simulators. Here, we examined over 200 VR navigation papers, and found that the most popular task used is the virtual analogue of the Morris water maze (VWM). Although we highlight the many advantages of using the VWM task, there are also some major difficulties related to the widespread use of this behavioural method. Despite the task's popularity, we demonstrate an inconsistency of use – particularly with respect to the environmental setup and procedures. Using different versions of the virtual water maze makes replication of findings and comparison of results across researchers very difficult. We suggest the need for protocol and design standardisation, alongside other difficulties that need to be addressed, if the virtual water maze is to become the 'gold standard' for human spatial research similar to its animal counterpart.

Keywords: spatial memory; spatial navigation; virtual reality; virtual maze; water maze.

Introduction

Navigation is a critical skill for many animals; the ability to recognize and recall locations is essential for everyday life. In many species, recalling where previous food has been stored and avoiding predators is crucial for survival. It is only when it is disrupted that we see serious consequences. It could be a life or death situation for most non-human animals; for example, birds with hippocampal damage demonstrate impaired homing/migratory ability and take longer to learn food locations (Bingman et al. 1988, 1990; Watanabe and Bischof 2004). It can be equally as devasting for humans, as observed in Alzheimer's Disease patients, who frequently report of disorientation or becoming lost (see Monacelli et al. 2003; Kalová, et al. 2005). Similarly, individuals with topographical disorientation suffer the inability to form a "cognitive map", which results in impairments in orientation regardless of the environments familiarity (see Bianchini et al. 2010; Iaria and Barton 2010).

Navigation assessment in animals and humans

The assessment of spatial navigation and memory in animal research has a rich tradition. Willard Small was one of the first to develop a maze for rodent learning over 100 years ago (Small 1901; see Commins 2018). Edward Tolman (1886–1959) continued this tradition and developed a variety of mazes including the starburst maze, which he used to demonstrate the idea of the cognitive map in rodents (Tolman 1949). Towards the end of the twentieth century, more sophisticated mazes were developed that allowed for the separation of spatial strategies and their neural substrates. For example, the T-maze takes the form a long narrow stem with two turning points at the end (as in the shape of a T). In this task rodents are tested for a range of cognitive processes, including the ability to recall cue-goal relationships, as well as, spatial working memory. Even when the hippocampus is removed or damaged, rats can still solve simple conditional or alternation reference tasks in the T-maze (see Deacon and Rawlins 2006; Deacon et al. 2001). The eight-arm radial arm maze (Olton and Samuelson 1976) has also been used extensively to

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examine a range of spatial processes including reference (Reisel and Banai 2002) and working memory (Frick et al. 1995). This maze contains a central circular arena from which eight tunnels or “arms” radiate outwards. The terminus of these arms contains a well in which a reward (such as food) can be placed. The ability of an animal to recall which arm contains the reward, relies heavily on spatial learning, memory, and the hippocampus (Bolhuis et al. 1986; Crusio et al. 1987). Both the T-maze and the eight-arm radial maze have also been used to separate response learning from place learning, showing that these strategies rely on very different brain structures (Packard and McGaugh 1996).

Circular open mazes were also developed, allowing more freedom to explore space. Initially designed to examine place learning theory (O’Keefe et al. 1975), this maze was soon adapted to different neurophysiological and behavioural studies (Barnes 1979; Bures and Fenton 2000). Thus, the neurobiological substrates of place learning and idiothetic and allothetic orientation were extensively studied in circular arenas, under different environmental conditions (Bures and Fenton 2000; Bures et al. 1997). Similarly, the water maze test developed by Richard Morris (1981) was proposed as an etiological based model of declarative memory and has been used extensively to examine a range of spatial processes including reference memory (Morris et al. 1990), working memory (Frick et al. 1995), and procedural memory (Whishaw 1985). In addition, the task has proven to be very useful in the examination of brain structures thought to underlie spatial navigation (McDonald and White 1994; Morris et al. 1982), as well as, being a standard test of memory in many disease models (see Commins and Kirby 2019). Given its extensive use, the Morris water maze (MWM; Morris 1984) is often considered as the “gold standard” test of animal learning and spatial memory. The general layout of this maze involves a circular pool filled approximately half-way with water. The animal is tasked with locating and recalling the position of an “escape platform”, which is submerged below the water surface in a fixed location and remains invisible to the subjects. The platform is generally camouflaged by colouring the water or making the platform from transparent materials. This facilitates the platform to have little or no visual presence in the pool; therefore, the location of the platform must be found and recalled (see Vorhees and Williams 2006) on subsequent trials. The maze provides a highly controlled environment for landmark manipulation, behavioural observation, and lesion studies. Hence, the animal can be trained with distal landmarks, proximal landmarks or with their trajectory alone (see Nunez 2008 for an outline of the procedure). In addition, a highly replicated finding using the MWM, is that damage to the hippocampus results in impaired allocentric (landmark) navigation (Morris et al. 1982; Sutherland and Rudy 1988). However, trajectory learning, or non-landmark dependant (egocentric) search strategies remain preserved (Eichenbaum et al. 1990; Vorhees and Williams 2006). Therefore, the flexibility of protocols and procedures provided by the MWM has led to it becoming the most popular test for spatial memory and navigation.

Assessment of spatial navigation in humans started to gain much interest towards the end of the last century. Some researchers, inspired by the animal research, began to assess spatial orientation in children and adults under different conditions using some of the classic spatial tasks or mazes (Aadland et al. 1985; Bohbot et al. 2002; Overman et al. 1996). Other studies tended to use more naturalistic environments (Barrash et al. 2000; Thorndyke and Hayes-Roth 1982). For example, Thorndyke and Hayes-Roth (1982), examined spatial recall by asking participants to learn a buildings layout from a map or by free-navigation around the building. Similar real-world navigation experiments have been used more recently to understand factors underlying human spatial learning and memory such as distance estimation (Commins et al. 2013), environmental orientation (Kimura et al. 2017) and spatial working memory (see Duff and Hampson 2001). Nevertheless, human spatial memory research has proven to be more difficult (see Diersch and Wolbers 2019). Large-scale navigational tasks are complex to control, standardise, and manipulate (see van der Ham et al. 2015). Additionally, data retrieval from ever-changing natural environments and constantly moving subjects can be difficult, resulting in very limited set of testable variables.

Virtual reality in spatial navigation research

With the growing popularity of Virtual Reality (VR) in scientific research over the last decades, researchers have made use of VR systems to assess human spatial memory and navigation in a much more accessible and controlled fashion (Maguire et al. 1997; Spiers and Maguire 2006). The translatability of virtual navigation has shown positive results. Navigation performance on a simplistic desktop programmes has repeatedly been shown to be predictive of real-world navigation performance (see Richardson et al. 1999; Sousa Santos et al. 2008). Similarly, results of real-world experiments have proven replicable with VR systems (such as Lloyd et al. 2009; Ruddle et al. 1997; Thorndyke and Hayes-Roth 1982). Although VR has been recognised as a useful method of examining spatial navigation in humans its experiences can sometimes suffer an absence of idiothetic, vestibular, and kinaesthetic information (see Ladouce et al. 2016; Park et al. 2018). However, the basic processes such as visual recognition and allothetic information processing (such as landmark and goal recognition) can be easily measured under highly controlled conditions (Bohil et al. 2011). Additionally, VR has revealed the importance of several emotional factors during exploratory behaviour in humans. For example, children with high levels of aggressiveness tend to withdraw from VR navigational studies (Rodriguez-Andres et al. 2018). Children with autism may also be less immersed or active during virtual navigation (Fornasari et al. 2013). In addition, children with high impulsivity could show a lack of inhibition in the virtual room, interacting very quickly with all the objects in the room or omitting some of the instructions (Cimadevilla et al. 2014). Though VR has provided an insight into several emotional contributions to navigation behaviour, it is important that researchers keep these in mind, as certain conditions or populations may respond differently to VR navigation.

In addition, VR applications have become successful tools for researching and helping clinical populations. VR applications involving navigational and non-navigational skillsets in brain injury patients has demonstrated positive results for assessment of deficit severity, rehabilitation, and also improving community living skills (Aida et al. 2018; Livingstone and Skelton 2007; Rose et al. 2005; Yip and Man 2009). Impaired spatial navigation has been detected in depressed patients using virtual reality platforms (see Cornwell et al. 2010) and aided the assessment of symptomology in psychotic conditions (Veling et al. 2014; Weniger and Irle 2008; Weniger et al. 2011). Assessment of spatial orientation may provide understanding of the topographical disorientation that occurs during normal aging and pathological aging. Thus, one of the most effective applications for VR is the detection of cognitive deficits during normal aging and in individuals with Alzheimer's disease (AD). Researchers have demonstrated that older adults show natural declines in navigation-related executive functions and spatial memory (see León et al. 2016; Moffat 2009; van der Ham and Claessen 2020). In addition, severe disruptions in spatial navigation abilities can be detected via VR navigation tasks in patients with Alzheimer's disease (Tu et al. 2017). Furthermore, detection of these dramatic declines could be used to monitor disease progression, delay the onset of severe symptomology and to help us understand the underlying mechanisms of the disease (see Cogné et al. 2017 for a review).

The use of VR has also facilitated our understanding of the neural correlates of spatial navigation, combining a VR application with a form of neurological measure (such as fMRI or electrophysiological recording of individual cells). Single cell recordings of place cells in humans during navigation has been made possible by using a VR task and epilepsy patients (Bischof and Boulanger 2003; Ekstrom et al. 2003; Jacobs et al. 2013). Invasive electroencephalography (iEEG) also involves the placement of electrodes deep into brain areas of interest with patient populations. Using this system, Kunz et al. (2019) demonstrated the ability to record landmark related spatial memory reactivation during stimulus-locked theta phases from electrodes in the anterior hippocampus. Standard EEG systems combined with VR have also been used to explore the relevance of theta oscillations during spatial navigation in humans (Boulanger et al. 2004; Sharma et al. 2017). Functional magnetic resonance imaging (fMRI) has been used to explore brain region activations during virtual spatial navigation, with focus on recognition and strategy selection (Maguire et al. 2006; Salgado-Pineda et al. 2016). However, these systems must be stationary, which may reduce immersive properties of some VR systems. Recently, mobile EEG systems have been developed with specific electrodes to record movement activity and other electrodes for standard neural activity. Their combination with an immersive VR environment well-facilitated to allow movement has demonstrated some promising compatibility and methodological approaches (see Ehinger et al. 2014). Despite some drawbacks, VR has proven vital for the successful, cost-effective, and controllable investigation of spatial navigation in humans.

Types of virtual navigation tasks

Though the use of VR has become a very popular tool for investigating spatial memory and navigation, the *type* of VR tasks used differs across laboratories (see Figure 1). Additionally, some high-end VR mazes can be expensive, designing original editions can be time-consuming and many versions have limited protocols (see Commins et al. 2020 for details). Many studies may use different versions, landmark types, and procedures (discussed below). This poses a problem when attempting to compare research across labs using different versions of the task. It also makes replicating experiments difficult, as some protocols are not clear or are only available upon purchasing the software.

To examine some of these issues in more detail and systematic fashion, using PubMed, Science Direct and Scopus databases we searched for the terms "Virtual Reality and Spatial Navigation" across the years 1998–2018. Spatial

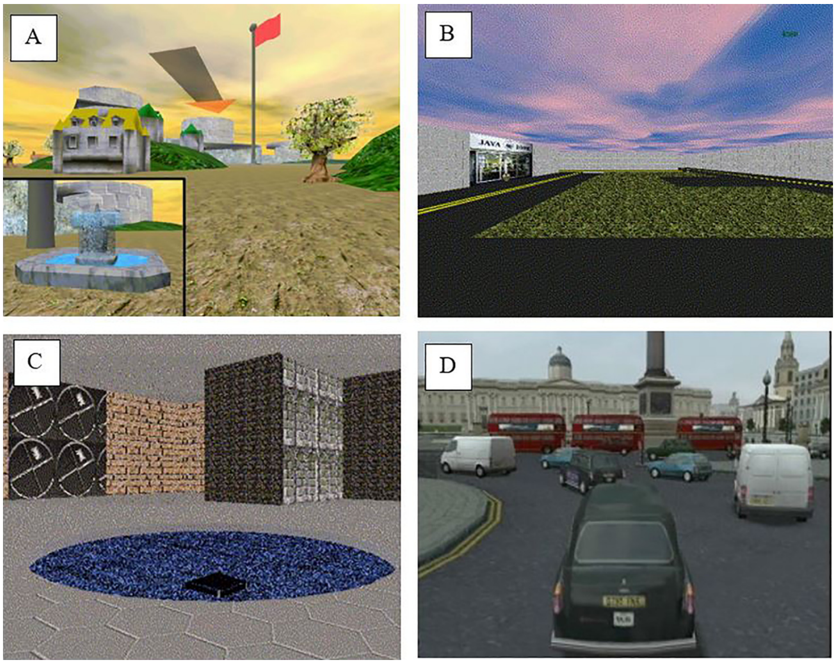

Figure 1: Examples of virtual mazes from the literature, such as the virtual island ‘memory island’ (A, from Piper et al. 2010); a virtual town (B, from Newman et al. 2007); an original virtual water maze (C, from Astur et al. 2004) and the virtual taxi simulator based in London (D, from Spiers and Maguire 2008).

Navigation incorporates a combination of cognitive skills such as learning, memory, and orientation. Choosing this search term delivers a strong source of papers from all the key areas of cognition under investigation, while placing a particular emphasis on navigation. The initial search delivered a total number of 1125 papers. Following removal of repetitions, reviews, and non-experimental studies, we included 203 papers for our first participant analysis. We then compared the types of ‘maze environments’ that were used. Twenty-two papers were excluded from *this* analysis as the description of the virtual environment used was not clear enough to categorise its type. A total of 178 papers were then used. Initial analysis of these papers revealed that the vast majority used healthy humans as participants (over 70% of papers examined). Patient population (individual case studies and groups) accounted for over 20%, with animals (mice and rats) acting as participants in just over 9% of the papers sampled (see Figure 2). Most papers involving animals and VR tended to investigate place, grid, and head direction cell activity (Aronov and Tank 2014; Schmidt-Hieber and Häusser 2013).

A breakdown of how these environments were defined is available in Table 1. If the authors made a clear description of the environment used, such as the virtual island task, it was given its own category. Where the environment was open to interpretation, such as a circular field in which participants searched for birds, it was counted under the most accurate category – such as “Open Outdoor Environment”. Many researchers have developed realistic scenarios, simulating buildings, streets or any other type of

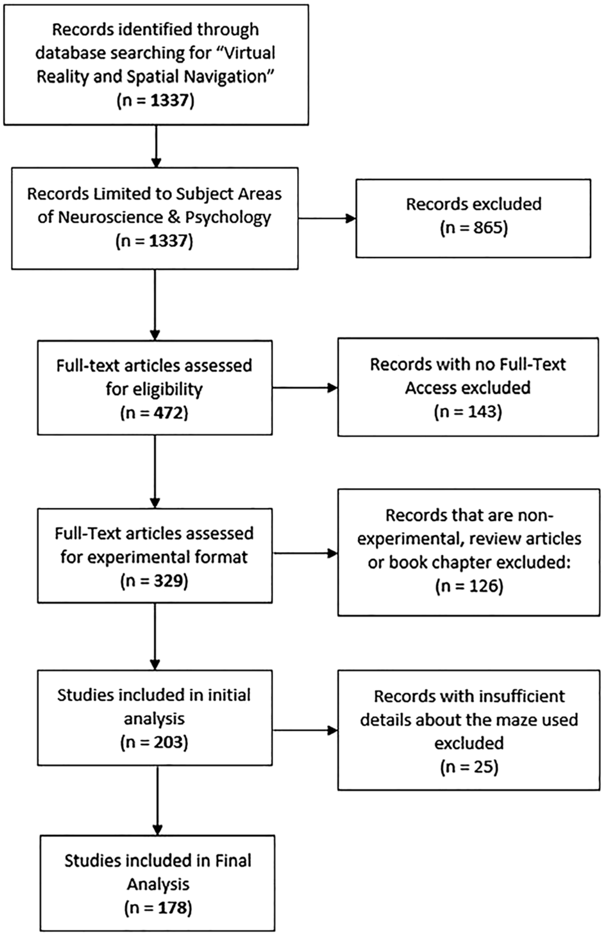

Figure 2: Number of papers analysed using Scopus search engine involving the key words “virtual reality spatial navigation” and provides details of the further reduction method.

Table 1: Definition criteria for different environment types used in papers.

Environment type	Description and criteria
Driving simulator	An environment in which the participant had to drive a vehicle and recall the route, such as a taxi driving game.
Indoor labyrinth	An environment with an escape at the end of a series of inter-linking corridors, based indoors, such as a tunnel.
Linear maze	A straight-line corridor or tunnel with no turns and featureless surroundings, usually used for rodent navigation
Open indoor arena	An indoor environment with open space to explore via free navigation, such as a large room or office
Open outdoor arena	An outdoor environment with open space to explore with free navigation, such as a park or field
Outdoor labyrinth	An environment with an escape at the end of a series of inter-linking passages with no ceiling, based outdoors, such as a hedge maze
Virtual city	A large-scale outdoor environment with distinguishable buildings (such as shops) or based on real large cities
Virtual hairpin	An environment with interconnected corridors of equal shape, size, and orientation
Virtual holeboard	An open, flat environment with evenly spaced holes containing rewards
Virtual house	An indoor space with two floors, with home furniture, specifically designed to replicate a home
Virtual island	An open outdoor island game, with buried treasure to find and island landmarks such as palm trees
Virtual multi-floor building	A large-scale indoor environment with more than two floors that can be freely explored, containing offices and rooms
Virtual museum	An open indoor environment with artefacts, exhibitions, and an array of interconnected areas, based off a museum
Virtual object recall	An open environment with randomly appearing and disappearing objects
Virtual plus maze	A cross shaped environment with two open and two closed arms
Virtual radial arm maze	An indoor environment with a circular open area with four to eight equally spaced corridors or "arms"
Virtual room(s)	An open indoor area, but with doors that allow entrance to different rooms with different furniture
Virtual star maze	A circular indoor area, with an internal star shaped fixture, with the five arms of the star acting as separate corridors
Virtual supermarket	An indoor interactive shopping game, based in a standard supermarket with products in different areas and a check-out
Virtual T-maze	An indoor T shaped maze with one linear corridor with two external corridors at the terminus
Virtual town	A small-scale outdoor environment with distinguishable buildings (such as shops) or based on real small towns
Virtual triangle maze	An indoor open area but specifically in the shape of a triangle, with landmarks on each angled point
Virtual water maze	An indoor or outdoor "pool" shaped environment in which a platform must be located or stated to be an analogue of the original Morris water maze

context where participants have to solve different spatial problems (Maguire et al. 1997; Wiener et al. 2020). Other efforts were made to adapt traditional spatial orientation mazes, previously used in rodents, to human research. In this respect, several traditional mazes have been adapted to VR assessment like T maze, hole-board maze, radial mazes or other mazes (Astur et al. 2004; Cánovas et al. 2008; Cimadevilla et al. 2011; Levy et al. 2005). Nevertheless, there is no doubt that the Morris water maze (MWM) as a "gold standard" method for studying spatial memory in rodent research has also been adapted to human research using VR-based techniques. Some virtual water maze (VWM) models incorporate landmarks from everyday life such as furniture (Folley et al. 2010), whilst in others, the original pool of the water maze is instead a circular desert island, in which participants must search for hidden treasure (Piper et al. 2010; Schoenfeld et al. 2010). Though there are many types of environments reported in the literature, most of them could be organised into four key categories (see Figure 3): Animal Analogues, Indoor environments, "Outdoor environments" and "Others".

The virtual water maze (VWM)

Across all the papers analysed, by far the most popular environment for examining spatial navigation and memory was found to be a virtual analogue of the Morris water maze, occurring in almost one fifth of the papers sampled

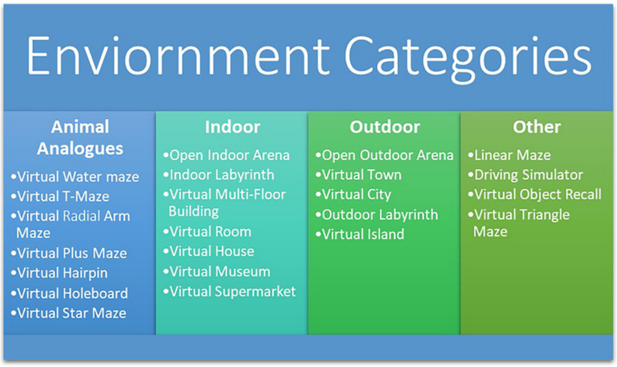

Figure 3: The types of mazes can be organised into four main categories: "Animal analogues", "Indoor", "Outdoor" and "Other".

(see Figure 4). We acknowledge that some items such as virtual city and virtual town could be considered as a single category, but, given that scale, distance, and context are important features for navigation (see Epstein et al. 2017) we have left them as two separate categories, classified under the outdoor heading (Figures 3 and 4). Furthermore, it is important to note that tasks are limited in what they can measure. Spatial navigation is a complex process involving many cognitive functions and abilities. All processes may not be examined by a single task. Indeed, while the VWM measures certain aspects of spatial ability very well, including landmark recognition, spatial orientation, and place learning (Vorhees and Williams 2006), other constructs such as path integration, audible cue recognition and route learning can be better studied using other tasks (for examples see Muffatto et al. 2016; Worsley et al. 2001). Therefore, it is perhaps not surprising the VWM task has emerged as the most popular task used. While we do not know the reason for this explicitly, we believe it is because of the task's translatability, simple design and good experimental control.

Translatability

One of the main advantages is the translatability of the task from animal research; this allows for more direct comparisons and is particularly useful when examining disease models. Most of the VWMs used in the literature have revealed similarities seen in the rodent version of the task. For example, like animal studies that demonstrate sex-differences (see Jones et al. 2003 for a review), males also spend more time than females in the target area during recall and learning (Astur et al. 2004; Woolley et al. 2010). The task has been effective and consistent for longitudinal and neural measurement studies on navigation and aging (Daugherty and Raz 2017; Daugherty et al. 2016; Zhong et al. 2017). Similar experimental designs and examinations have all been previously attempted with the animal version of the task. However, several factors that influence navigation in the rodent version of the task are removed when made virtual, such as motivation and physical locomotion (Devan et al. 2018). Despite this, spatial performance seems to be similar across rodents and humans when directly compared on a real and VWM respectively (Schoenfeld et al. 2017). It is generally difficult to incorporate these factors, regardless of the virtual environment chosen.

However, it does lack ecological validity when compared to virtual towns or cities. Some virtual towns are based on real-life towns (van der Ham et al. 2010) and though virtual cities are larger scale, they can still closely replicate real-life cities, such as London or Rome (Ferrara et al. 2008; Maguire et al. 2006). Familiar environments produced virtually are rarely as intensive as in real-life, which is a good compromise for aiding ecological validity whilst retaining practicality. Recently, a novel mobile task, 'Sea Hero Quest' has demonstrated real-world ecological validity, with correlations between the task and real-world performances in participants (Coutrot et al. 2019). But in

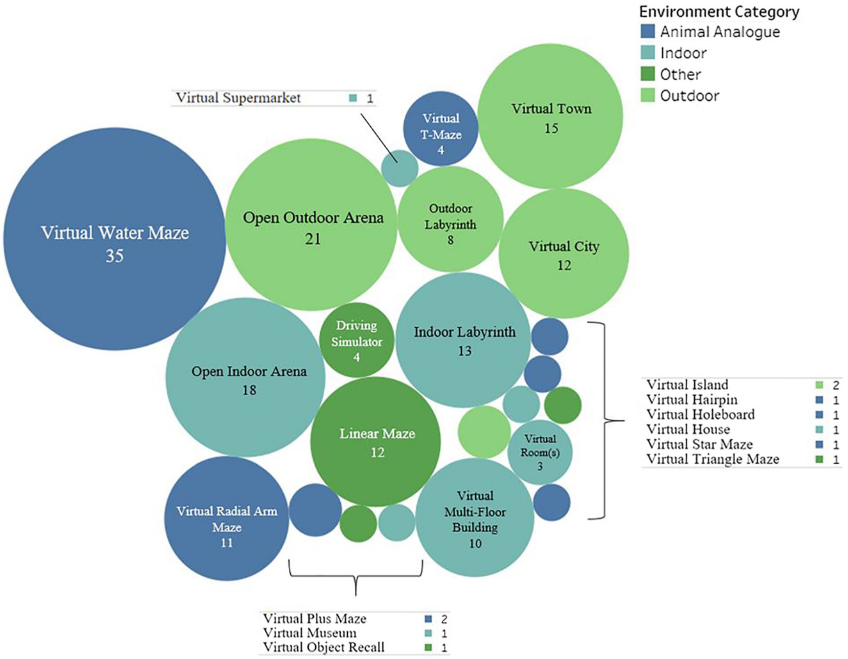

Figure 4: Bubble chart showing the number of virtual environments used in a sample of papers involving the key words "virtual reality spatial navigation" for data visualisation purposes. The bubble size represents its percentage of occurrence throughout the papers and is colour coded based on the environment categories defined in Figure 3. Text is only shown in bubbles for environments occurring three or more times, with occurrences ranging from one to a maximum of 35.

this task, participants navigate a boat around animated lakes and valleys. Therefore, it could even be suggested that the behaviours involved in navigation may be more important than the context in which they are carried out.

Simple design and good experimental control

The water maze has an effective and simple design, which carries over into its virtual analogues. There is very little occurring on screen for participants, with the lack of intense visual stimuli and sparse or simple landmarks allowing for greater engagement and less disorientation (Ruddle et al. 1997; Vinson 1999). The distinct landmarks and enclosed, open arena used in these VWMs promotes rapid learning of the task, which may take much longer in complex towns or cities. Younger adults find using some VWM software very easy (see Commins et al. 2020); but older adults may take longer to adapt. The VWM has also effective use with clinical populations, demonstrating correlations between performance on a VWM and lower scores on the Montreal Cognitive assessment (MoCA, Rogers Castillo et al. 2017). Comparable deficits were found during learning/recall between rodents expressing human amyloid precursor protein (hAPP) and mild cognitive impaired (MCI) patients (Possin et al. 2016). The simple design of the VWM facilitates a user-friendly task for use with patients in the clinic.

The VWM also provides a large amount of experimental control, with manipulations of environments, landmarks, and protocols completed with ease. However, it is important bear in mind that circular arenas and mazes, like the MWM, were developed to simplify the environment and decipher the neurobiological bases of behaviour. The animal version of the task is not exempt from variabilities across labs either. Though most use circular tanks, not all may use blackout curtains, and rooms may contain features that cannot be controlled for such as overhead lights, cameras, and cables, which may incidentally act as landmarks. The control of landmarks available and examination of the strategies displayed by participants allows researchers to determine how subjects solve the task, and which neural circuits are involved. This is particularly important in the clinic, where spatial tasks have been recently considered essential for identifying and determining the progression from healthy aging to neurodegeneration (Diersch and Wolbers 2019). Though a more ecologically valid test could be used with humans, the VWMs environmental simplicity, ease of use and substantial amount of translatable research completed with animals, makes the task desirable for it to become a standardised tool both in research and the clinic.

Challenges with the virtual water maze

The nature of VR software allows for researchers to deploy creative, realistic, and immersive environments and protocols with ease. However, if the virtual analogue of the water maze is to become the “gold standard” for human spatial research and possibly adapted for use in the clinic, there are number of very practical issues that would need to be first addressed. For example, if head mounted displays are used, cost, and ease-of-use for all cohorts and especially vulnerable populations should be addressed. Furthermore, methodologies and protocols should be standardised – there are some major differences across labs with respect to environmental setups and procedural approaches. Such issues are not as applicable with the animal version of the water maze task as circular tanks and black-out curtains rarely differ from one another. Though there are some methodological problems and discrepancies across the animal literature, many researchers operate to the basic guidelines originally proposed by Morris (1984) and further expanded by incredibly descriptive and detailed papers such as Vorhees and Williams (2006, 2014).

Different environment setups

It seems that one consistent feature of the virtual versions of the water maze used throughout the literature is the shape of the pool. Most papers declare that the environment used is “circular” or a “pool”. However, unless screenshots of the maze are provided, researchers must take on the assumption that referring to the environment as a “pool”, implies that the pool is also circular. Using different shaped environments, such as squares and triangles, is mostly done to look at the influence of geometrical landmarks such as corners or textures found on the environment itself (Bécu et al. 2020; Commins et al. 2020; Redhead et al. 2013). Using a circular arena removes the influence of geometrical landmarks and is most alike the animal version of the task (see Figure 5 for pools taken from the sample studies and more recent papers).

However, many researchers do not provide the essential measurements of the pool. There is often a large difference comparing participant navigation in a very small arena compared to a very large arena as the time taken and path distance to reach the goal location (common VWM

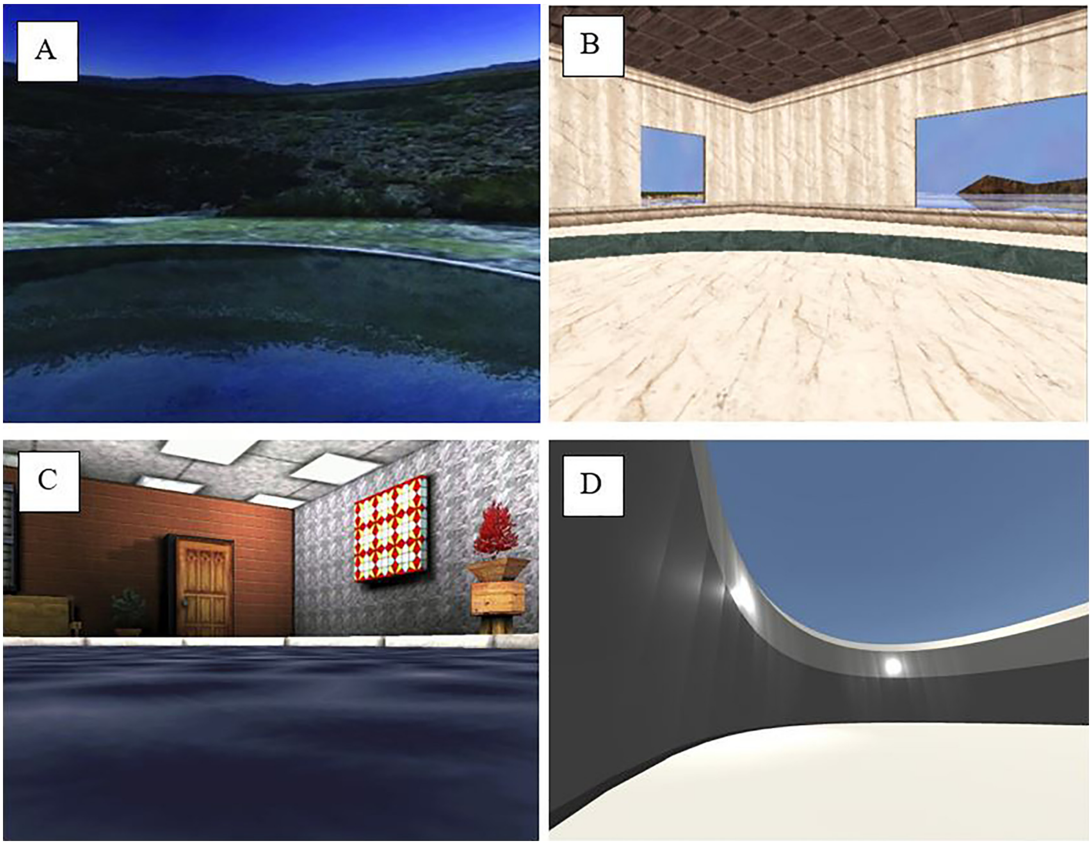

Figure 5: Examples of virtual water maze layouts from the current literature, such as a modern one with forest and mountain landmarks (A, from Machado et al. 2019); an indoor water maze with a window (B, from Livingstone-Lee et al. 2011); a water maze in a room with furniture (C, from Newhouse et al. 2007) and our own open-access maze, 'NavWell' (D, see Commins et al. 2020).

measures) differs depending on how large the arena actually is. In an attempt to provide some context to the size of the pool used, researchers can provide measurements in virtual units or virtual metres. Nevertheless, unlike real-world measurements in metres, virtual metres may differ depending on the software used; and it is unclear if virtual units are the same as virtual metres. One way to demonstrate the size of the arena used is to provide the traversal time (time taken to navigate, at a standard speed, from one side of the pool to the other, see Hamilton and Sutherland 1999). However, providing this and not explaining how these traversal times relate to the contextual size of the arena, makes the measurements redundant. Alternatively, the time it takes to perform one full rotation of viewpoint may also be useful (see Redhead and Hamilton 2009). From Table 2, several papers do not actually provide an arena size at all or may refer to a previous paper from another lab. Often only one type of size measurement is given, some vague (such as "large" arena) and other precise within one measurement domain (pool: 40 m, room: 75 × 75 × 17.5, wall: 1 m high).

Another inconsistency seems to be the relative size of the platform or goal location. Though some researchers are clear with platform size measurements, it is difficult to work out the actual size of the target area used when the entire environment size is not provided (see examples in Table 2). Particularly in the context of the popular "water" maze alternative: Virtual Island, in which participants must search for hidden treasure on a generally round shaped sand island. However, the size of the hidden treasure and its location size are difficult to assess in most cases. Nevertheless, the most important thing is the size of the platform or goal, as different sized goal locations would make the recall of the place more or less difficult. It would be essential to provide the size of the platform as percentage of the total environment, alongside the platforms shape.

Environmental boundaries are reported to affect spatial navigation, with boundary-specific cells being reported in humans (Lee et al. 2018). The existence of these cells and the possibility of boundaries being integrated or utilised as landmarks would indicate that this is also an

Table 2: An example of a more in-depth literature comparison of VWM environment design.

Paper	Year	Arena shape	Indoor/outdoor	Platform size/shape	Arena size
Astur et al.	2002	"Pool"	Indoor (pool in a room)	No details provided	No details provided
Daugherty et al.	2015	"Pool"	Indoor (pool in a room)	Approx. 12% of arena size	No details provided
Hamilton and Sutherland	1999	Circular	Indoor (square room; pool wall 15% of room height)	Square (approx. 1.75% of the pool surface area)	Traversal 4 s full rotation 2.5 s
Hamilton et al.	2009	Circular	Indoor	0.66 Vu × 0.66 Vu (approx. 20%)	16 Vu × 16 Vu × 3 Vu
Moffat and Resnick	2002	Circular	Indoors (irregularly shaped room)	Square (no size given)	No details provided
Mueller et al.	2008	Circular	Indoor (very large square room)	No details provided	"Large" appeared 40 m in diameter with 1 m high wall
Rodgers et al.	2012	Circular	Indoor	No details provided	"Large"
Schoenfeld et al.	2010	Virtual island (round)	Outdoor	Hidden treasure	No details provided
Skelton et al.	2006	Round	Indoor with view of outdoor	Round (5 m in diameter visible as a disk 0.1 m thick)	Pool: 40 m, room: 75 × 75 × 17.5, wall: 1 m high
Skelton et al.	2000	Circular	Indoor	Square (7 m)	Pool: 40 m, room: 60 × 60 × 15, wall: 3 m high

We chose some important factors discussed above to compare, that are known to differ between labs and maze software.

important issue to highlight for standardisation. Thus, it is essential to understand whether the actual pool (arena in which navigation can take place) is inside or outside. Almost all researchers provide this detail either directly in-text, or indirectly via images (e.g. Skelton et al. 2006), as it is also essential for understanding whether the landmarks used are distal or proximal. As discussed previously, other virtual environments can be defined by outdoor and indoor categories. However, it should be a detail about the environment that is provided regardless of the software being used, particularly when the room itself is immersive enough to act as a landmark. This is important to understand how landmarks are being processed during navigation.

Procedure

Researchers using the animal version of the MWM generally all follow the original procedure outlined by Morris (1984) and further developed by Vorhees and Williams (2006, 2014). However, as the VWM is still a relatively novel technique for examining spatial cognition in humans, the same baseline protocols do not exist. This is mainly due to the variety of commercial versions of the VWM, which are immersive and well-designed, but may be costly for labs with insufficient funding. This can lead researchers to design and produce their own VWM software. In turn, this saves on cost or may be necessary because many of the commercial versions are not capable of manipulating variables the researchers may be interested in. Because of this ongoing trend, there is variability and inconsistencies across VWM procedures, as different groups programme their software differently or may later switch to a commercial version instead.

One of the main problems that arises and where the VWM differs from its animal version, is the fact that it is inconvenient and difficult to train humans in a similar fashion to animals. Rodents would usually be given multiple trials a day for a number of days; usually four trials across four to six days on average (Commins and Kirby 2019). Longer protocols that reflect the animal literature are probably not needed, as humans learn faster than their rodent counterparts. However, this is not something all researchers are adapting, particularly when trying to replicate and compare with rodent studies. As it is difficult to get humans to return on several days for participation (particularly for imaging or electrophysiological studies), the multiple trial blocks are usually completed on the same day. There is a lack of consistency in the literature surrounding the total number of trials required. For example, some participants receive six blocks of three trials (Hamilton et al. 2002) or seven blocks of four trials each (Driscoll et al. 2005). In some cases, participants can be given one block of 10 trials (Goodrich-Hunsaker et al. 2010; see Table 3 for more comparisons). Related to this, starting positions should be alternating cardinal points in a semi-random order, similar to those recommended for animals by Vorhees and Williams (2006). Researchers may choose to use the N, E, S and W cardinal points, alternating them in blocks of four to avoid participants learning the sequence (see method used by Skelton et al. 2006 and Newhouse et

Table 3: An example of a more in-depth literature comparisons of VWM procedures and protocols.

Paper	Year	Trial types	Trial length	Trial number	Starting positions
Antonova et al.	2011	Visible & hidden	30 s per stage & 15 s rest	Six trials consisting of acquisition, recall, rest, visual control, and rest.	"Different" (no details)
Driscoll et al.	2005	Hidden & visible	60 s per trial, 10 s ITI on platform	Seven blocks of four trials	Varied (no details)
Goodrich-Hunsaker et al.	2010	Practice, visible & hidden	180 s per trial then "guided" to platform	One practice trial, Four visible trial & 10 hidden trials	Alternated cardinal points: NWSE walls
Hamilton et al.	2002	Hidden (visible if not located)	60 s per trial, 10 s ITI on platform	Six blocks of three trials	Randomised but not repeated
Hamilton et al.	2003	Hidden & visible	60 s per trial, 5 s ITI on platform, 2 s rest	Five blocks of Four trials (hidden) & two blocks of eight trials (visible)	Four pseudorandom points around perimeter
Herting and Nagel	2012	Practice, hidden & visible	Unlimited time, 10 s ITI on platform	One practice (hidden), six learning (hidden) & one visible	Six randomly assigned each trial
Kallai et al.	2005	Practice, visible & hidden	180 s per trial, no ITI	One practice room, two visible trials & eight hidden trials	N/A
Newhouse et al.	2007	Hidden & visible	60 s per trial then "guided" to platform, 3 s free swimming, 5 s ITI	Four blocks of four trials	Randomly assigned. Not repeated in a block: NSEW
Shipman and Astur	2008	Hidden, visible, practice & fixation (crosshair gaze)	33 s per trial, 474 s per task, 23 s per fixation	15 hidden trial, five repetitions of three conditions	Four Pseudorandom points

We chose some important factors discussed above to compare, that are known to differ between labs and maze software.

al. 2007). Much of the VWM literature has adopted the same protocol as the animal version of the task. However, it is important that researchers include this detail when describing their methodology, rather than listing starting positions as "varied" or "different" (see Table 3). Another major inconsistency across VWM literature is the length of the acquisition trials. Standard trial length for the animal protocol is usually between 1 and 2 min (see D'Hooge and De Deyn 2001; Vorhees and Williams 2006). However, there is a lot of variation with respect to the VMW. The range of 1–2 min is a popular trial length used in the current human literature (see Table 3). However, this should and can be adjusted depending on the participant group and non-behavioural recordings being carried out. For example, patient populations or older adults may need to be given more time to search (Daugherty et al. 2016; Skelton et al. 2006). On the other hand, participants performing the task in an MRI scanner may need to be given shorter trials (e.g. Folley et al. 2010).

It is important to have an interval between trials regardless of the number used. It allows the animal to learn more about the environment and the goals spatial location, as well as, preventing fatigue. For humans, it provides a break from constant engagement with VR or screen-time too which may help them improve their focus and performance (see Ribeiro et al. 2020). It is conventional for this break to be introduced as an Inter-Trial Interval (ITI). The most common ITI used for animals and humans is approximately 10 s (Vorhees and Williams 2006). However, some VWM researchers report no ITI at all (e.g. Kallai et al. 2005). Others switch to a blank "rest period" screen for 15 s (Antonova et al. 2011). Further details can be seen in Table 3. The difficulty with this is that participants have no time to take in information about their place and its relation to cues in the environment; which helps to reinforce place learning. Particularly, this ITI should be taken when the participant has located the goal, causing them to become stationary but capable of examining the environment visually (as rats would do in the MWM). The reason shorter ITI times are used may be due to human participants possessing full control over the task (see Mueller et al. 2008). Some participants may rush to get to the next trial, whereas others may wish to have extended breaks (particularly if using VR gear). Nonetheless, it is also vital to ensure enough rest time is given to suit certain individuals; particularly vulnerable groups. However, for consistency across research, it is better to enforce a standard ITI time when running VWM procedure if possible. Cross-maze comparisons could be made easier were there equal break times, as we are unaware if this additional exposure to the environment during a break facilitates better learning.

Additionally, animals in the MWM are always "guided" to the platform when they have failed to locate its position during a timed trial. This procedure is not commonly employed with humans (see Table 3). If the maze software allows; participants should be placed at the goal position after an unsuccessful trial. They should be informed that it is located here, and be allowed to familiarise themselves with the position (see Commins et al. 2020). Alternatively, the software can switch to a "free-swim" mode, and the participant can be guided by the researcher or the software (see Goodrich-Hunsaker et al. 2010). In other cases, the platform raises, revealing its location to participants to swim and reach it (Astur et al. 2004; Cánovas et al. 2008). This protocol is recommended to train the animal on the purpose of the task and could speed up spatial learning (Nunez 2008). Not guiding humans to the platform would make their performance difficult to compare with animals that were repeatedly shown the platforms position during learning. It would also encourage participants to learn the goals spatial location and not a standard route to the goal. Additionally, if a smaller number of trials are used, guiding participants to the platform will help with learning over a shorter time period.

Other challenges

There are some additional challenges that have transferred over to tasks virtual analogue. One such challenge is that of "probe" or recall trials. The timing of the recall trials can depend on the lab, with the most common usually given to animals 24 h after the last learning trial, to assess reference memory (Barnhart et al. 2015; Vorhees and Williams 2006). However, delayed probe trials could sometimes reveal differences that an immediate probe trial would not (see Cimadevilla et al. 2004). It is usually convenient for both researchers and participants to administer the probe trials just after the final learning trial. Particularly for experiments in which participants spend considerable time in MRI or MEG setups, or vulnerable patients whose availability is low. However, the type of memory being examined here may be difficult to determine, as it may be the memory from the previous learning trial rather than the entire learning process (Vorhees and Williams 2006). Therefore, the type of VWM used needs to have the facility to manipulate the type of probe trials that are given, depending on the type of memory being examined. For example, to examine working memory, the position of the platforms location must be capable of being changed across trials. The probe trial must also reflect this after each training session. Additionally, the type of learning being examine is also important. For example, a learning phase with a visible platform that does not end the task (false-goal) and one that does (true-goal), would examine visual discrimination learning (see Voorhees and Williams 2006). This must be reflected in the probe trial also, which may be limited by certain VWM software. Manipulating cued learning and spatial associations, requires the VWM software to be capable of adding and removing landmarks during probe trials. Consequently, some labs may approach these protocols differently, depending on what the VWM is capable of achieving. This could lead to some inconsistencies that may be important for comparing between recall trials across labs.

Another minor issue surrounds the use of control procedures. Most animal versions of the task use an alternative version of the acquisition trials, in which the platform is clearly visible or clearly marked with an intra-maze cue, such as a coloured flag or light (see Voorhees and Williams 2006; Williams et al. 2003). Animals usually participate in a control task, along with the main experimental task (Barry and Commins 2019). Some researchers use the same approach with humans (Laczó et al. 2010; Redhead and Hamilton 2009) or include a control free-swim condition (Woolley et al. 2013). Others compare participants across groups based on general cognitive ability, through the use of already standardised paper and pen tests, such as the Trail Making Tests and the MoCA (Commins et al. 2020; Korthauer et al. 2016; Meade et al. 2019). It is important that some form of control protocol is used, but its methods and results should be made available, to help guide future research. This is increasingly important for neural research, as it is important to understand brain activity at a controlled baseline during navigation, particularly when examining changes to the environment or comparing patients to matched controls (Kober and Neuper 2011; Slobounov et al. 2015). Particularly because baseline activity in one VWM may differ to baseline activity in another, depending on the VWMs immmersiveness, landmarks or protocol. Similarly, these control measures should link in with the memory or learning type under examination, and whether the population contains vulnerable individuals, such as patients or older adults. Therefore, recommended control measures for different populations and/or the concept being examined should be in place, providing group comparison consistency regardless of the VWM used.

Additionally, there is also the issue of task difficulty. Some participants struggle to master the task, which can result in making the task easier by adding easier controls (such as a joystick) or even by adding intra-maze cues. Pretraining, if any, can also differ substantially from paper to paper. It can be used to familiarise older adults with the technology (solving the issue mentioned above) or to help the participant be more comfortable in an fMRI or EEG setup. This should also be standardised to produce comparable measures from the main MWM performance.

Why is this important?

The purpose of this short review is to highlight some of the emerging problems that are beginning to appear in the VWM literature. The two main factors are environment design and protocol. Though many protocols have reasoning behind their use e.g. no landmarks for investigating path integration or including visual practice trials for older adults. It is important that their use is standardised. A particular protocol in one VWM, may impact behaviour differently in another VWM with different design (e.g. a virtual town and a virtual city). This, in turn, may impact replication across labs. The same is true for two differing protocols in the same environment (e.g. a 5 s ITI and a 10 s ITI would allow for more rest but also additional learning if participants remain in the environment). Therefore, it is essential for researchers to clearly explain their VWM design and protocol.

To provide a minor but revealing example, we will briefly look at two papers that investigated patients of amnestic mild cognitive impairment (aMCI) using two differently designed versions of a virtual radial arm maze. One group of researchers found aMCI patients to demonstrate impaired reference memory but not working memory compared to controls (Lee et al. 2014). The other researchers demonstrated that aMCI patients had worse navigation and memory performance overall compared to controls (Weniger et al. 2011). Both tasks are the same in principal. However, they appear visually different compared to each other using the figures provided. One version of the maze in Weniger et al. (2011) had no landmarks, and another contained overt landmarks (e.g. cars or rivers). Lee et al. (2014) had landmarks also, but not much detail was provided other than the fact they were coloured objects and visual cues. Considering a large percentage of controls and aMCI patients reported memorising landmarks as their main navigation strategy in Weniger et al. (2011) (Controls: 70%; aMCI patients: 90%) surely the type and positioning of landmarks here is important. Furthermore, Lee et al. found that aMCI converters had more severe reference memory impairments than non-converters. Weniger et al. (2011) found no difference between converter and non-converters on their task. This group had a maximum 5-min exploration to find one target in the maze used. Lee et al. (2014), had no limit, but time latency for trials was recorded with the highest average being only 5 min. These researchers had an ITI of 10 s, whereas Weniger et al. (2011) do not mention the inclusion of an ITI at all. In the Lee et al. (2014) paper, participants had three different targets to locate per trial whereas in Weniger et al. (2011) there was only one main target in a much larger area. These papers consist of well-designed studies that make an essential contribution to the field. But we think this does highlight the advantages of a similar protocol and environment design. It would be useful if researchers could apply a *similar* protocol to a *particular* environment design, including for, and not limited to participant type or the type of memory being examined. The environment is the most important feature involved in navigation, and by ruling this out as a reason behind reported impairments, observed deficits and particular behaviours, we can generate more robust and replicable spatial navigation research.

Conclusion

Virtual reality is a popular tool for spatial navigation research, animals and humans alike. VR seems to present itself in the literature in many forms, such as fully immersive 3D with oculus rift technology (see Commins et al. 2020; Machado et al. 2019) or simple but immersive computer-based 2D versions (Antonova et al. 2011; Astur et al. 2004). However, for spatial navigation research, the virtual environment that is navigated through, remains one of the most important factors. Interestingly, the types of VR environments used in spatial navigation experiments differ greatly. They span from virtual islands to taxi driving simulators and virtual towns or cities. Many involve a maze-type environment, with many virtual analogues of popular animal mazes such as the T-Maze and Radial Arm Maze. However, it is rather fitting that the most popular VR environment is based off the most popular animal assessment tool; the Morris water maze (Morris 1984). Though the water maze has had many years to adapt standardised setups and protocols, its virtual analogue has only started the journey. As explored above, many of these VWM setups use different environment shapes, sizes, and platforms with varying trials, intervals, and starting positions. This can make cross-comparison difficult, and animal translatability even more problematic. There are a multitude of reasons why this has occurred, possibly down to different software capabilities, cost, and experimental setups. It is clear when these problems are examined and different VWMs are compared, there are some real discrepancies across research.

The purpose of this paper is to highlight the emerging problems within VR spatial navigation research with humans. The VWM has many advantages and may be slowly paving its way towards the most popular tool for navigation research with humans. Nevertheless, it is vital to emphasize some of the problem's researchers may be facing now, as the number of custom or widely differing mazes increases, the VWM as a tool may lose its overall reliability. From the above review, it may be necessary to have a set of standardised protocols for the VWM, much like those available for its animal counterpart (Vorhees and Williams 2006). Though procedures can be standardised, one element of the Morris water maze that is difficult to control across labs can be its appearance. The benefit of using a virtual version of the task, unlike a physical maze, is that its appearance can be designed and redesigned to abide by certain protocols if necessary. Additionally, the use of just a small number of VWMs across different research groups would be ideal, but difficult. The release of open-source mazes, such as NavWell form our own lab (Commins et al. 2020) will hopefully encourage replication across labs. The answer to standardisation is not straightforward, as research with a VWM comes with numerous difficulties and influential variables. We hope this short review can highlight some issues that are beginning to emerge, but also, the crucial but challenging opportunity, for the VWM to become the 'gold standard' test for examining human spatial navigation.

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