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Conflicts of Interest

The authors have no conflicts of interest to declare:

We certify that no party having a direct interest in the results of the research supporting this article has or will confer a benefit on us or on any organization with which we are associated AND, if applicable, we certify that all financial and material support for this research (e.g., NIH or NHS grants) and work are clearly identified in the title page of the manuscript.

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Comprehensive Neuropsychological Assessment of Cognitive Functioning of Adults with Lower Limb Amputation in Rehabilitation

Objective: To establish a comprehensive profile of cognitive functioning in people engaged in lower limb amputation (LLA) rehabilitation.

Design: Cross-sectional study as part of a longitudinal prospective cohort.

Setting: A national, tertiary, rehabilitation hospital.

Participants: Adult volunteer participants (N=87) referred for comprehensive rehabilitation for major LLA were sampled from 207 consecutive admissions. Participants with both vascular (n=69) and non-vascular (n=18) LLA aetiologies were included.

Interventions: Not applicable

Main Outcome Measure(s): Demographic and health information, and a battery of standardised neuropsychological assessments

Results: Compared to normative data, impairment was evident in overall cognitive functioning ($p \leq .003$). Impairment was also evident in particular areas, including reasoning, psychomotor function, information processing, attention, memory, language/naming, visuospatial functions, and executive functions (all $p \leq .003$ Holm-corrected). There were also higher frequencies of impaired functions across most aspects of functioning in this group, compared to expected frequencies in normative data ($p \leq .003$ Holm-corrected). There were no significant differences in cognitive functioning between participants of vascular and non-vascular LLA aetiology.

Conclusions: Findings support the need for cognitive screening at rehabilitation admission regardless of aetiology. Administration of comprehensive neuropsychological assessment with a battery sensitive to vascular cognitive impairment is recommended in some cases, to generate an accurate and precise understanding of relative strengths and weaknesses in cognitive functioning. Cognitive functioning is a potential intervention point for improvement of rehabilitation outcomes for those with LLA and further research is warranted in this area.

Key Words: Amputation; cognition; lower extremity; neuropsychology; rehabilitation research

List of abbreviations

- BADS: Behavioural Assessment of the Dysexecutive Syndrome
- CVLT-II SF: California Verbal Learning Test II Short Form
- D-KEFS: Delis Kaplan Executive Function System
- FrSBe: Frontal Systems Behavior Scale – self-rated
- LLA: lower limb amputation
- MCI: mild cognitive impairment
- MoCA: Montreal Cognitive Assessment
- PVD: peripheral vascular disease
- RBANS: Repeatable Battery for the Assessment of Neuropsychological Status
- TEA: Test of Everyday Attention
- VCI: vascular cognitive impairment
- VOSP: Visual Object and Spatial Perception Battery
- WAIS-IV: Wechsler Adult Intelligence Scales-IV
- WMS-IV: Wechsler Memory Scale-IV

In economically developed countries, most major lower limb amputations (LLA) result from dysvascularity, i.e. peripheral vascular disease (PVD) and diabetes mellitus [1]. People with LLA (PwLLA) are at greater risk of having or developing impaired cognitive functioning [2], with high prevalence of dysvascularity as a precipitating factor in LLA likely underlying this risk. PVD is a marker for generalised cardiovascular and cerebrovascular pathology, and has been linked to impaired cognitive functioning and vascular cognitive impairment (VCI) [3–5]. Overall cognitive functioning, processing speed, attention, immediate and delayed memory, naming, visuospatial construction, and executive functions are impaired in VCI [6]. Diabetes has been associated with a similar profile of impairment[7]. Furthermore, the increasing age at which most LLA are carried out itself presents increasing risk of cognitive impairment and dementia [8]. In essence, LLA risk factors – dysvascularity and advanced age – are shared risk factors for cognitive impairment. Impaired cognitive functioning may explain a proportion of the variance in rehabilitation outcomes [9]; yet relatively little research has considered cognitive functioning in PwLLA [2]. While there is some evidence of impaired memory [10], information processing [11], and executive functioning deficits [10,11] in PwLLA, a comprehensive understanding has been hampered by limitations of methodology and scope of the extant research literature.

Profiles of cognitive functioning are heterogeneous; people have variable relative strengths and weaknesses across different aspects of functioning, the degree of such strengths and weaknesses also varies. Most previous research however has relied on simple categorical definitions of cognitive functioning (e.g. [12–16]), including unspecified dementia diagnoses, rather than standardised neuropsychological assessment. This approach neglects the range of functioning in the LLA population, ultimately limiting understanding of the range of potential contributors to rehabilitation outcomes. Furthermore, studies examining cognitive profiles have generally used cognitive screens or narrow assessment batteries, which do not capture

the breadth of functioning or are insensitive to VCI [10,17,18]. In some cases, reporting was not sufficient to make determinations regarding the profile [12,18]. Drawing conclusions from other studies is limited by sample sizes or research designs that preclude generalisation [11,19]. Comparisons between patients of vascular and non-vascular LLA aetiology are also lacking, limiting our understanding of the general profile of functioning in the LLA rehabilitation population.

Recent work with a large sample with LLA (N=1086) examined self-reported cognitive concerns (i.e. difficulties in functioning) [20]. Respondents reported significantly more cognitive concerns than a general population normative sample, regardless of age or aetiology. However, self-report and third party observation may not be reliable indicators of cognitive functioning. Persons with executive functioning difficulties may lack insight into their own cognitive functioning and behaviour. Additionally, difficulties with aspects of cognitive functioning can be masked, for example by intact language production skills. With greater scope than cognitive screens, comprehensive neuropsychological assessment can elucidate the breadth and depth of cognitive strengths and weaknesses, thus assisting treatment or rehabilitation planning[21].

The purpose of this study was to generate a comprehensive neuropsychological profile of people who attended rehabilitation at a national rehabilitation hospital following LLA. The aim was to describe cognitive functioning in terms of a) whether LLA rehabilitation participants' assessment scores differed from normative means, and b) the proportions of the sample with scores in the borderline or impaired ranges of functioning. Cognitive functions assessed included overall cognitive functioning, reasoning, psychomotor speed, information processing, attention, memory, visuospatial perception and construction, language, and executive function, as well as estimated premorbid intellectual ability. A

secondary aim was to investigate differences between participants with vascular and non-vascular aetiologies.

Methods

Design

This cross-sectional study forms part of a longitudinal prospective cohort study investigating cognitive functioning and rehabilitation outcomes in PwLLA enrolled in a comprehensive LLA rehabilitation programme at a Commission for Accreditation of Rehabilitation Facilities (CARF) -accredited rehabilitation hospital.

Participants

Inclusion criteria were: presence of a major LLA (i.e. unilateral or bilateral from ankle to hip level), English language fluency, age≥18 years. Exclusion criteria were: major upper limb amputation (i.e. wrist disarticulation or above; participants with transphalangeal or partial hand amputation were not excluded provided they could manipulate assessment materials), or being too medically unwell.

Eighty-seven participants were recruited. Of 207 consecutive admissions over two years, 3 were excluded as medically unwell, 1 was non-English speaking, and 116 declined. Participants gave written, informed consent prior to participation. The hospital's Ethics Committee approved this research.

Measures

Demographic and clinical data were collected from healthcare records. Distress was assessed using Hospital Anxiety and Depression Scale total scores [22,23]. The battery of standardised neuropsychological assessments was selected to provide a comprehensive profile of cognitive functioning and impairment, be sensitive to VCI, and limit burden on participants. It and aspects of cognitive functioning examined are noted in table 2. Higher scores indicate higher levels of functioning, with exception of the Frontal Systems Behaviour Rating Scale (FrSBe), for which lower scores indicate better self-rated functioning. All measures were age standardised, with the FrSBe also gender normed.

Procedure

The majority of participants engaged in at least two assessment sessions, lasting on average 50 minutes. Where timetables allowed, sessions up to approx. 110 minutes with a short break in the middle were conducted. Sessions continued until the battery (approx. 3.5 hours) was completed, or discontinued due to participants declining further participation, limitations on timetable availability, or early discharge from rehabilitation. Assessments were undertaken while participants were engaged in a busy rehabilitation programme, and were delivered across sessions in an order that minimised the risk of assessments interfering with each other. As completion rates differed, the order of test administration was altered to prioritise completion of measures of overall cognitive functioning in the first instance (e.g. RBANS), then measures tapping into each of one of the following domains: attention, memory, executive function, and then the remainder of the battery. Some assessments were completed as part of routine clinical assessment. Participants were referred to a senior clinical

neuropsychologist (FOK) if they requested feedback on assessments or in instances of distress.

Analysis

To examine relationships between demographic and clinical variables and neuropsychological assessments, including whether scores differed between vascular and nonvascular amputation aetiologies, independent samples t-tests, Mann-Whitney U tests, and Spearman rho correlations were used. In assessing whether LLA rehabilitation participants' assessment scores differed from normative means, one-sample t-tests were used. Sample means were compared against the means and standard deviations of published normative values for each assessment. Similar analyses have been used previously[20,24], and allow for an inferential estimation of whether and how cognitive functioning in (this whole sample of) PwLLA differs from the general population.

To estimate the proportions of PwLLA in rehabilitation programmes that might require particular rehabilitative attention due to difficulties with various aspects of cognitive functioning, separate chi-square analyses investigated with the distribution of scores at each of three levels (where normative values were available). The levels were impaired ($z \leq -2.0$; scale scores 1-3; $\leq 2^{nd}$ percentile), borderline ($-1.99 \leq z \leq -1.5$; scale scores 4-5; $\leq 7^{th}$ percentile approx.) and not impaired. This classification of 'impairment' is used in the Wechsler classification system[25]; the z=-1.5 borderline classification has been used in studies of mild cognitive impairment (MCI) [26–28]. Two assessments were exceptions: FrSBe [29] (borderline: $60 \geq T \leq 64$; impaired: $T \geq 65$) and VOSP Position Discrimination (borderline: raw score 18/20; impaired: raw score ≤17/20).

Holm's method of correction for multiple comparisons [30,31] was employed on a family-wise basis. Effect sizes reported are Cohen's *d* (small≥.2, medium≥.5, large≥.8). Data were analysed with IBM SPSS Statistics version 21.

Results

Sample demographic and clinical characteristics are summarised in Table 1. Participants with dysvascular LLA (PVD or diabetes) were significantly older (n=69, M=62.93, SD=12.02, range=33–86) than the non-vascular group (n=18, M=41.89, SD=15.13, range=21–73) ($t(85)=6.26$, $p<.001$). Groups did not differ in education, gender, marital status, amputation level, number of comorbidities, distress, or length of stay. The sample was slightly younger than the group of all potential participants attending LLA rehabilitation at the recruitment site (annual M=60 to 63 during recruitment years). Other demographic or clinical information of non-participants was not available.

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INSERT TABLE 1 ABOUT HERE

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Cognitive functioning was impaired, both generally and across specific domains, as evident in the significantly lower performance of the sample on the clear majority of aspects of cognitive functioning assessed relative to normative means. Results of this main analysis

are summarized in table 2, which also provides information on normative means and standard deviations for reference. This sample did not differ from the normative population in estimated premorbid intellectual ability. Overall cognitive functioning was significantly lower (RBANS Total Index; d=-.9), and the mean MoCA score of 22.9 (SD=3.99) was below the cut-off (<24 [32]) for suspected cognitive impairment. The sample scored significantly lower on all three reasoning assessments ($d \leq$-.52) and on psychomotor speed (d=-.72). For information processing, significantly lower scores were evident on colour-naming (D-KEFS Color-Word Interference Condition 1(Colour Naming), d=-.7), and difficult, time-pressured tasks (RBANS Coding, d=-1.25; WAIS-IV Symbol Search, d=-1.03), but not word reading (D-KEFS Color-Word Interference Condition 2 (Word Reading), d=-.29). All assessments of focused and sustained attention were significantly lower (-.69$\geq d \geq$-1.45), but differences in attention span and divided attention were non-significant (RBANS Digit Span, d=.12; TEA Telephone Search While Counting, d=-.22). Both immediate list learning scores were significantly lower (-.42$\geq d \geq$-.8). The sample fared better on immediate story memory, with a non-significant difference on a shorter story (RBANS Immediate Story Memory, d=-.24), and a significant difference of small effect size for longer stories (WMS-IV Logical Memory I, d=-.47). There was no significant difference in recall after a 1 minute delay following four trials of a verbal list (CVLT-II SF short delay free recall, d=-.3). All aspects of recall after longer delays (circa 20+ minutes), were significantly lower (-.44$\geq d \geq$-.73). Delayed recognition scores were also significantly lower (RBANS List Recognition, d=-.58), even when cues were provided (CVLT-II SF cued recall, d=-.84). No difference was evident in confrontational naming of everyday objects (RBANS Naming, d=-.23). The GNT included less common items, and the mean raw score (16.95, SD=6.44) corresponded to approximately the 25th percentile. Participants fared better on visuospatial perception (VOSP Position Discrimination M=18.98, SD=1.61, within the 'pass' range; RBANS Line Orientation, d=-

.17) than construction (RBANS Figure Copy, *d*=-.54). Of the core aspects of executive functioning, significantly lower scores were evident in inhibition (D-KEFS Color-Word Interference Condition 3 (Color-Word Switching), *d*=-.76), cognitive flexibility (D-KEFS Trail Making Test Condition 5 (Number-Letter Switching), *d*=-1.05), and all aspects of verbal fluency (-.42≥*d*≥-.72). Working memory, which did not differ, was an exception (WAIS-IV Digit Span, *d*=-.15, ns). The planning (BADS Zoo Map) mean score corresponded to borderline impaired functioning. Self-rated executive and frontal lobe dysfunction (including apathy, behavioural disinhibition, dysexecutive functioning) was significantly higher (FrSBe Self-Rated Total, *d*=.59).

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INSERT TABLE 2 ABOUT HERE

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Significantly higher proportions of the sample had borderline and impaired scores compared to normative populations across the cognitive functioning spectrum (see table 3). This included overall cognitive functioning (RBANS Total Index, 34% of scores), visual abstract reasoning (WAIS-IV Matrix Reasoning, 21%), psychomotor speed (D-KEFS Trail Making Test Condition 5 (motor speed), 19%), and complex, time pressured information processing (RBANS Coding, 58%; WAIS-IV Symbol Search 33%). This was also the case for all aspects of attention (range=11-41%) except divided attention, all aspects of immediate and delayed memory (range=21-41%), confrontational naming (RBANS Naming, 17%), visuospatial perception (line orientation, 22%), and construction (figure copy, 43%). Similar results were found for a range of executive functions including inhibition (38%), cognitive flexibility (47%), and verbal fluency (category and phonemic, 19-23%). Additionally, a

significantly higher proportion had scores in the borderline or extremely low range for estimated premorbid intellectual functioning (WTAR, 22%). 52.6% of MoCA scores fell at or below the selected cut off (<24). The VOSP Position Discrimination task was failed by 28% of those who completed the measure. For planning (BADS Zoo Map), 88% of scores were in the borderline or impaired ranges. FrSBe self-ratings were above the threshold for executive and frontal lobe dysfunction (including apathy and behavioural disinhibition) for 45.5% of those who completed the measure.

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INSERT TABLE 3 ABOUT HERE

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Mann-Whitney U tests indicated no significant differences in assessment scores between aetiology groups (scores for the vascular and non-vascular groups are provided in table 3 for comparative purposes, with additional information in table S1 [online supplement]). Amputation level, length of stay, marital status, and distress (HADS) were unrelated to test scores. Older age was significantly related to lower MoCA (r_s=-.503, p<.001) and lower RBANS Line Orientation (visuospatial perception, r_s=-.443, p<.001) scores. More comorbidities (dichotomised as two or fewer versus three or more) related to lower RBANS Coding scores (information processing, $t(71)$=3.576, p=.001). There were no differences in assessment scores (or a range of demographic and clinical variables) between a group which completed ≥90% (n=25) of the assessments and those who completed <90% (n = 62), with one exception: RBANS Immediate Story Memory ($t(65.236)$=-3.439, p=.043).

Discussion

This study was the first to employ such a broad battery of standardised neuropsychological assessments, selected purposefully to be sensitive to common features of VCI, to provide a profile of cognitive functioning in admissions to rehabilitation programmes. The profile is one of high degree and prevalence of impairment in overall cognitive functioning as well as widespread impairment across domains, including reasoning, information processing, attention, immediate memory/learning, delayed recall and recognition memory, naming less commonplace objects, visuospatial perception and construction, and executive functions including cognitive flexibility/set-shifting, inhibition, verbal fluency, and planning. Particular difficulties, in both magnitude and prevalence of difficulty, were evident in overall cognitive functioning; processing speed(especially under time pressure); focusing attention and sustaining concentration; learning verbal information, and; recalling newly learned information even with cuing. Among executive functions, cognitive flexibility (switching between tasks and thinking creatively), and planning presented particular difficulties.

The results support research suggesting increased overall susceptibility to cognitive impairment [2], impaired processing speed and executive functioning [11] and reduced immediate and delayed list recall and verbal fluency across time in dysvascular LLA [10], and similar

findings in PVD [3]. Importantly, this study evidences impairment across a much wider range of cognitive domains.

In economically developed countries, persons with dysvascular LLA predominate in LLA rehabilitation programmes. Impairment observed in these individuals is likely linked to cerebrovascular diseases. The observed profile was largely consistent with VCI; difficulties with overall cognitive functioning with particularly high frequency of impairments of processing speed, executive functioning, attention, and memory. Yet, LLA aetiology does not map reliably onto impairment status. The similarly poor performance of non-vascular LLA participants across the full range of assessments raises questions about cognitive functioning in this group. Previous research on found that people with traumatic LLA were no less concerned about their cognitive functioning than those with vascular LLA [20], though how subjective concerns map onto and objective assessments of cognitive functioning is uncertain. Demographic or clinical factors, including distress, did not explain the lack of difference between aetiologies. One possible explanation is the presence of vascular risk factors; a third of the non-vascular group had cardiovascular comorbidities. Additional risk of traumatic amputation in dysvascularity has been reported previously [33] (vascular insufficiency likely being a contributory factor).

Half of participants scored below the selected cut-off for cognitive impairment (MoCA <24), suggesting that comprehensive neuropsychological assessment may be appropriate for at least half of LLA rehabilitation programme admissions. Cut-off sensitivity and specificity [32] suggest that approximately a quarter of participants could meet MCI criteria. A reliable and valid cognitive screen, sensitive to VCI, should be administered on admission to LLA rehabilitation, even to those with non-vascular LLA aetiology. Individuals' patterns of strengths and impairments varied with complexity which could not have been captured with categorical measures alone (e.g. screening pass/fail). More accurate and precise

306 understandings of patients' relative or actual strengths and weaknesses are possible by
307 twinning cognitive screening as standard with comprehensive neuropsychological assessment
308 as required. A non-exhaustive list of instances suggesting benefit in neuropsychological
309 assessment includes: scoring below or near a cognitive screen cut off; notable discrepancies
310 between scores in different domains on a cognitive screen; functional difficulties suggestive
311 of cognitive difficulties; and self-reported or other-reported cognitive difficulties.

312 While there are clear resource implications for implementing neuropsychological
313 assessment, potential benefits include earlier and better understanding of why difficulties may
314 arise with particular tasks, functioning, or activities of daily living [34,35], prosthesis use or
315 mobility [36–39], self-management and compliance with medical regimen [40,41], or social
316 integration and community participation [39]. Additionally, declines in cognitive functioning
317 may have implications for sustaining achieved goals in the longer term. Prospective
318 associations between cognitive functioning and rehabilitation outcomes suggest an influence
319 on longer-term outcomes [36,39]. Timely assessment would improve potential for earlier
320 intervention to mitigate these difficulties with concomitant benefits of reduced healthcare
321 expenditure and resource use.

322 Research is required to examine whether lower premorbid cognitive functioning or
323 intellectual ability confer additional amputation risk. While mean estimated premorbid
324 intellectual ability did not differ from normative values, a greater proportion of this sample
325 was in the borderline and extremely low ranges. Self-management of later-stage PVD carries
326 a cognitive burden and requires motivation. Brief cognitive screening for at-risk persons
327 could contribute to LLA prevention.

328 This study evidences impairment across attention, memory, and executive functions
329 which could reasonably be considered particularly important for rehabilitation and outcomes.

Intact cognitive functioning is likely to be important in learning to effectively and safely don, doff, transfer and ambulate with, and maintain prostheses, but LLA rehabilitation now extends beyond prosthetic provision and training [9,42] . Some people achieve functional independence and adjust well after LLA, yet others do not [9]. Reintegration into community living and social roles may depend somewhat on cognitive functions and their successful application. Some additional cognitive burdens for PwLLA include planning, activity organization, and memory for prosthetic procedures. Understanding precipitant factors of good and poor activity performance, participation, and overall adjustment to limb loss will assist in rehabilitation programme development and optimization. Cognitive rehabilitation has already yielded promising results in facilitating prosthesis use [19] and its efficacy in improving other outcomes should be researched. Clinicians supporting emotional and psychological adjustment to amputation and prosthesis use should be mindful of the cognitive resources required and the potential for impaired cognitive functioning even in non-dysvascular LLA. Lastly, how cognitive functioning impacts on the process of engagement in LLA rehabilitation itself and subsequent rehabilitation outcomes [43] warrants examination.

Study Limitations

Differing completion rates for each of the neuropsychological assessments are a limitation of the present study. Assessments were undertaken during routine, busy rehabilitation programme schedules. Heterogeneous completion rates related to restrictions in participant scheduling and research availability, early discharge, declining to continue (often citing fatigue), and the time required for battery completion. Fractionation of assessment sessions due to fatigue and scheduling difficulties was previously reported in the only other study to report comparably comprehensive neuropsychological assessment in PwLLA [11].

The sample was slightly younger than all PwLLA attending rehabilitation at the recruitment site. Additionally, those who agreed to participate may have represented a more engaged and motivated patient subset. Indeed, VCI has been associated with elevated apathy [44]. Thus, the profile presented may underestimate cognitive impairment present in the LLA rehabilitation population. Differing aetiology group sizes reflected the preponderance of dysvascular LLA common in industrialized countries, but make it difficult to draw firm conclusions about the relationship between cognitive functioning and aetiology. Multi-site recruitment with matched cases may facilitate recruitment of those less likely to participate and aetiological comparisons. Further research could also recruit an appropriate control group, for example persons with acquired physical impairment but without VCI risk.

Time of day (TOD) of testing may affect assessment performance across several neuropsychological variables of interest. Older age has been associated with lower performance in the afternoon compared to the morning, and vice versa for younger age [45]. While it was not possible to control for TOD effects within this study, this could be considered for future investigations.

Previous examinations of working memory in LLA have employed similar digit span measures to assess working memory, with similar null findings [10,11,39]. Digit forward and backward conditions incorporated in the WAIS-IV digit span test, measures of attention span and short term memory respectively [46], potentially confounded assessment. Alternatives should be considered, e.g. digit ordered conditions alone, or *n*-back tasks[47].

Conclusions

Difficulties with cognitive functioning in LLA are many, varied, and not confined to vascular LLA. A true representation of cognitive functioning is best obtained with a comprehensive

neuropsychological assessment. Ultimately, increased knowledge about cognitive functioning in LLA could assist in supporting patients in rehabilitation and help them to optimise rehabilitation outcomes and overall quality of life.

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INCLUDE TABLE S1 AS ONLINE SUPPLEMENT

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Table 1

Demographic and Clinical Characteristics of the Sample

Variable	Level	n	% or M (SD)	Range
Age (years)			58.6 (15.3)	21 - 86
Gender	Male	65	74.7	
	Female	22	25.3	
Education (years)			12.5 (3.4)	4 – 23
Marital status	Married/cohabiting	44	51	
	Not married	43	49	
Amputation	Below knee [†]	34	39.0	
	Above knee	41	47.1	
	Bilateral	12	13.8	
Aetiology	Vascular [‡]	69	79.3	
	Non-vascular [§]	18	20.7	
Comorbidities	0 to 2	45	51.7	
	3+	42	48.3	
Months since amputation			23.5 (73.7)	1 – 535
Length of stay (weeks)			8.4 (4.1)	1 – 22
Distress (HADS)		55	10.96	0 – 35

NOTE. HADS = Hospital Anxiety and Distress Scale [22]

[†] Includes n=1 through-knee amputation

[‡] PVD, diabetes, osteomyelitis with comorbid diabetes

[§] Trauma, cancer, intravenous drug use

Table 2

Neuropsychological Assessment Scores

Domain	Assessment	Score Type	Normative M (SD)	N	M	Median	SD	Min to Max	*t* (df)	Cohen's *d*	Effect size
Estimated premorbid intellectual ability	WTAR Standard Score	ST	100 (15)	50	96.2	99.5	19.35	50 to 123	-1.388 (49)	-0.2	NS (small)
Overall cognitive functioning	MoCA	Raw	n/a †	58	22.9	23	3.99	9 to 30	n/a	n/a	n/a
	RBANS Total Index	ST	100 (15)	72	84.96	86	16.9	45 to 121	-7.605 (72) *	-0.9	Large
Reasoning	WAIS-IV Block Design	SCL	10 (3)	60	8.2	8	3.18	1 to 17	-4.388 (59) *	-0.57	Medium
	WAIS-IV Similarities	SCL	10 (3)	60	8.13	8	2.9	1 to 15	-4.982 (59) *	-0.64	Medium
	WAIS-IV Matrix Reasoning	SCL	10 (3)	56	8.34	8	3.16	2 to 15	-3.928 (55) *	-0.52	Medium
Psychomotor speed	D-KEFS TMT condition 5 (motor speed)	SCL	10 (3)	42	7.71	8	3.16	1 to 12	-4.693 (42) *	-0.72	Medium
Information processing	D-KEFS CWIT condition 1 (color naming)	SCL	10 (3)	52	8.23	8	2.52	3 to 15	-5.068 (51) *	-0.7	Large
	D-KEFS CWIT condition 2	SCL	10 (3)	52	9.29	9.5	2.49	1 to 13	-2.059 (51)	-0.29	NS (small)

	(word reading)										
	RBANS Coding	Z	0 (1)	73	-1.77	-1.65	1.41	-5.08 to +1.54	-10.699 (72) *	-1.25	Large
	WAIS-IV Symbol Search	SCL	10 (3)	60	6.98	6.5	2.94	1 to 18	-7.940 (59) *	-1.03	Large
Attention	RBANS Digit Span	Z	0 (1)	76	0.07	0.18	1.12	-2.47 to +2.29	1.014 (75)	0.12	NS (negligible)
	D-KEFS TMT condition 1 (visual scanning)	SCL	10 (3)	52	7.85	9	3.1	1 to 13	-5.007 (51) *	-0.69	Medium
	D-KEFS TMT condition 2 (number sequencing)	SCL	10 (3)	54	7.17	8	3.88	1 to 14	-5.367 (53) *	-0.73	Medium
	D-KEFS TMT condition 3 (letter sequencing)	SCL	10 (3)	53	6.81	8	3.93	1 to 14	-5.911 (52) *	-0.81	Large
	TEA Telephone Search	SCL	10 (3)	32	5.84	6	2.96	1 to 13	-7.934 (31) *	-1.45	Large
	TEA Telephone Search With Counting	SCL	10 (3)	32	9.13	8.5	4.14	1 to 19	-1.195 (31)	-0.22	NS (small)
Memory	RBANS List Learning	Z	0 (1)	76	-1.03	-0.96	1.2	-3.88 to +1.38	-6.940 (75) *	-0.8	Large
	CVLT-II SF Free Recall T-Score (list)	T	50 (10)	56	44.95	47	11.97	18 to 66	-3.161 (55) *	-0.42	Medium

	RBANS Immediate Story Memory	Z	0 (1)	76	-0.41	-0.11	1.54	-4.65 to +1.76	-2.070 (75)	-0.24	NS (small)
	WMS-IV Logical Memory I (story)	SCL	10 (3)	59	8.07	8	4.15	1 to 16	-3.578 (58) *	-0.47	Small
	CVLT-II SF Short Delay Recall (list)	Z	0 (1)	53	-0.41	-0.5	1.37	-2.5 to 4.0	-2.151 (52)	-0.3	NS (small)
	RBANS Delayed List Recall	Z	0 (1)	76	-0.9	-0.83	1.19	-3.61 to +1.39	-6.351 (75) *	-0.73	Medium
	CVLT-II SF Long Delay Recall (list)	Z	0 (1)	52	-0.62	-0.5	1.04	-2.5 to 2.0	-4.281 (51) *	-0.59	Medium
	RBANS Delayed Story Recall	Z	0 (1)	76	-0.79	-0.5	1.32	-3.68 to +0.91	-4.973 (75) *	-0.57	Medium
	WMS-IV Logical Memory II (story)	SCL	10 (3)	59	7.68	8	4.07	1 to 16	-4.377 (58) *	-0.57	Medium
	RBANS Figure Recall	Z	0 (1)	77	-0.55	-0.59	1.14	-3.48 to +1.97	-3.867 (76) *	-0.44	Small
	CVLT-II SF Long Delay Cued Recall	Z	0 (1)	52	-0.86	-0.5	1.06	-3.0 to 1.0	-6.044 (51) *	-0.84	Large
	RBANS List Recognition	Z	0 (1)	76	-2.18	-1.17	3.64	-25.43 to +0.67	-5.051 (75) *	-0.58	Medium
Language	RBANS Picture Naming	Z	0 (1)	76	-0.41	0.55	1.79	-7.4 to +1	-2.044 (75)	-0.23	NS (small)

	GNT raw score	Raw	n/a †	39	16.59	18	6.44	3 to 27	n/a		
Visuospatial cognition	RBANS Figure Copy	Z	0 (1)	77	-1.11	-0.85	2.05	-8 to +1.29	-4.745 (76) *	-0.54	Medium
	RBANS Line Orientation	Z	0 (1)	77	-0.28	0.12	1.68	-5.5 to +4.62	-1.458 (76)	-0.17	Negligible
	VOSP Position Discrimination raw	Raw	n/a †	43	18.98	20	1.61	12 to 20	n/a	n/a	n/a
Executive functions	WAIS-IV Digit Span	SCL	10 (3)	62	9.52	3.2	10	2 to 17	-1.192 (61)	-0.15	Negligible
	D-KEFS CWIT condition 3 (colour-word switching)	SCL	10 (3)	50	7	8	3.95	1 to 13	-5.365 (49) *	-0.76	Medium
	D-KEFS TMT condition 4 (number-letter switching)	SCL	10 (3)	53	5.81	6	3.99	1 to 13	-7.651 (52) *	-1.05	Large
	RBANS Semantic Fluency	Z	0 (1)	76	-0.91	-1	1.22	-3 to +2	-6.309 (75) *	-0.72	Medium
	D-KEFS VFT condition 1 (category fluency)	SCL	10 (3)	57	8.42	8	3.74	3 to 17	-3.186 (56) *	-0.42	Small
	D-KEFS VFT condition 2 (letter fluency)	SCL	10 (3)	57	8.12	8	3.73	2 to 19	-3.802 (56) *	-0.5	Medium
	BADS Zoo Map	Raw	n/a †	41	n/a	2	n/a	1 to 6	n/a	n/a	n/a
	FrSBe self	T	50 (10)	35	59.8	53	16.66	33 to	3.481	0.59	Medium

rated total	103	(34) *

NOTE. BADS = Behavioural Assessment of the Dysexecutive Syndrome [38]; CVLT-II SF = California Verbal Learning Test – II Short Form [39]; D-KEFS = Delis-Kaplan Executive Function System (CWIT = Color-Word Interference Test; TMT = Trail Making Test; VFT = Verbal Fluency Test) [40]; FrSBe = Frontal Systems Behavior Scale [21]; GNT = Graded Naming Test [41]; MoCA = Montreal Cognitive Assessment [42]; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status [43]; TEA = Test of Everyday Attention [44]; VOSP = Visual Object and Space Perception Battery [45]; WAIS-IV = Wechsler Adult Intelligence Scales – IV [46]; WMS-IV = Wechsler Memory Scales – IV [47]; WTAR = Wechsler Test of Adult Reading [48]

* significant ($p \leq .003$) after the Holm method of correction for multiple comparisons was employed

† Raw scores: MoCA and GNT each have a possible raw scores ranging from 0 to 30. VOSP possible scores range from 0–20 (pass≥19, pass borderline=18, fail/impaired≤17/20). BADS zoo map possible scores range from 1 to 7 (pro-rated ordinal scale).

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Table 3

Neuropsychological Assessments: Proportions of Scores in the Borderline or Impaired Ranges

Domain	Assessment	N	% borderline	% impaired	% impaired or border.	*p*	χ^2 (df = 2)	Aetiology	N	% impaired	% borderline	% impaired or border.
Estimated premorbid intellectual ability	WTAR Standard Score	50	12	10	22	.001*	22.11	VAS	38	10.5	13.2	23.7
								NV	12	8.3	8.3	16.7
Overall cognitive functioning	MoCA	58	n/a	n/a	52.6 †	n/a	n/a	VAS	49	n/a	n/a	61.2
								NV	9	n/a	n/a	11.1
	RBANS Total Index	72	12.3	21.9	34.2	<.001*	158.47	VAS	58	24.1	13.8	37.9
								NV	15	13.3	6.7	20.0
Reasoning	WAIS-IV Block Design	60	13.3	5	18.3	0.017	11.86	VAS	48	4.2	16.7	20.8
								NV	12	8.3	0	8.3
	WAIS-IV Similarities	60	10	6.7	16.7	0.021	10.14	VAS	48	8.3	6.3	14.6
								NV	12	0	25	25
	WAIS-IV Matrix Reasoning	56	17.9	3.6	21.4	.003*	20.46	VAS	44	4.5	18.2	22.7
								NV	12	0	16.7	16.7
Psychomotor speed	D-KEFS TMT condition 5 (motor speed)	42	7.1	11.9	19	.001*	21.64	VAS	32	12.5	6.3	18.8
								NV	10	10	10	20
Information processing	D-KEFS CWIT condition 1 (color naming)	52	7.7	3.8	11.5	0.438	1.76	VAS	40	2.5	10	12.5
								NV	12	8.3	0	8.3
	D-KEFS CWIT	52	1.9	1.9	3.8	0.676	1.04	VAS	40	2.5	2.5	5

	condition 2 (word reading)										
	RBANS Coding	73	16.4	41.1	57.5	<.001*	597.05	NV	12	0	0	0
								VAS	58	46.6	19	65.5
	WAIS-IV Symbol Search	60	26.7	6.7	33.3	<.001*	67.34	NV	15	20	6.7	26.7
								VAS	49	6.1	30.6	36.7
Attention	RBANS Digit Span	76	7.9	2.6	10.5	<.001*	1.53	NV	11	9.1	9.1	18.2
								VAS	60	3.3	5	8.3
	D-KEFS TMT condition 1 (visual scanning)	52	9.6	9.6	19.2	.001*	18.13	NV	16	0	18.8	18.8
								VAS	42	11.9	11.9	23.8
	D-KEFS TMT condition 2 (number sequencing)	54	5.6	24.1	29.6	<.001*	134.37	NV	10	0	0	0
								VAS	43	30.2	7	37.2
	D-KEFS TMT condition 3 (letter sequencing)	53	5.7	30.2	35.8	<.001*	215.36	NV	11	0	0	0
								VAS	42	33.3	4.8	38.1
	TEA Telephone Search	32	17.2	24.1	41.4	<.001*	83.44	NV	11	18.2	9.1	27.3
								VAS	24	26.1	21.7	47.8
	TEA Telephone Search With Counting	32	10.3	3.4	13.8	0.393	2.11	NV	8	25	0	25
								VAS	24	4.3	13	17.3
Memory	RBANS List Learning	76	7.9	27.6	35.5	<.001*	257.58	NV	8	12.5	0	12.5
								VAS	60	30	5	35

							NV	16	18.8	18.8	37.5
CVLT-II SF Free Recall T-Score (list)	56	7.1	14.3	21.4	<.001*	44.03	VAS	44	15.9	9.1	25
							NV	12	8.3	0	8.3
RBANS Immediate Story Memory	76	6.9	16.1	23	<.001*	106.79	VAS	60	23.3	5	28.3
							NV	16	0	18.8	18.8
WMS-IV Logical Memory I (story)	59	16.9	16.9	33.9	<.001*	87.36	VAS	48	16.7	16.7	33.3
							NV	11	18.2	18.2	36.4
CVLT-II SF Short Delay Recall (list)	53	11.3	15.1	26.4	<.001*	51.82	VAS	42	16.7	11.9	28.6
							NV	11	9.1	9.1	18.2
RBANS Delayed List Recall	76	17.1	14.5	31.6	<.001*	86.34	VAS	60	15	18.3	33.3
							NV	16	12.5	12.5	25
CVLT-II SF Long Delay Recall (list)	52	7.7	19.2	26.9	<.001*	80.17	VAS	42	19	7.1	26.2
							NV	10	20	10	30
RBANS Delayed Story Recall	76	2.6	21.1	23.7	<.001*	141.07	VAS	60	25	3.3	28.3
							NV	16	6.3	0	6.3
WMS-IV Logical Memory II (story)	59	5.1	28.8	33.9	<.001*	216.69	VAS	48	29.2	2.1	31.3
							NV	11	27.3	18.2	45.5
RBANS Figure Recall	77	13	9.1	22.1	<.001*	31.07	VAS	62	8.1	16.1	24.2
							NV	15	13.3	0	13.3
CVLT-II SF	52	11.5	25	36.5	<.001*	146.87	VAS	42	28.6	11.9	40.5

	Long Delay Cued Recall										
							NV	10	10	10	20
	RBANS List Recognition	76	2.6	38.2	40.8	<.001*	506.99	VAS	60	40	3.3	43.3
								NV	16	31.3	0	31.3
Language	RBANS Picture Naming	76	1.1	15.8	17.1	<.001*	75.15	VAS	60	15	1.7	16.7
								NV	16	18.8	0	18.8
	GNT raw score	39	n/a	n/a	n/a	n/a	n/a	VAS	30	n/a	n/a	n/a
								NV	9	n/a	n/a	n/a
Visuospatial cognition	RBANS Figure Copy	77	14.3	28.6	42.9	<.001*	295.75	VAS	62	33.9	16.1	50
								NV	15	6.7	6.7	13.3
	RBANS Line Orientation	77	5.2	16.9	22.1	<.001*	87.17	VAS	61	21.3	6.6	27.9
								NV	16	0	0	0
	VOSP Position Discrimination raw	43	14	14	28	n/a	n/a	VAS	34	17.6	11.8	29.4
								NV	9	0	22.2	22.2
Executive functions	WAIS-IV Digit Span	62	6.5	4.8	11.3	0.265	2.88	VAS	50	4	8	12
								NV	12	8.3	0	8.3
	D-KEFS CWIT condition 3 (colour-word switching)	50	12	26	38	<.001*	154.07	VAS	39	30.8	15.4	46.2
								NV	11	9.1	0	9.1
	D-KEFS TMT condition 4 (number-letter switching)	53	7.5	39.6	47.2	<.001*	384.98	VAS	42	42.9	7.1	50
								NV	11	27.3	9.1	36.4
	RBANS Semantic	76	18.4	22.4	40.8	<.001*	194.36	VAS	60	20	18.3	38.3

Fluency											
							NV	16	31.3	18.8	50
D-KEFS VFT condition 1 (category fluency)	57	17.5	8.8	26.3	<.001*	33.25	VAS	45	8.9	20	28.9
							NV	12	8.3	8.3	16.7
D-KEFS VFT condition 2 (letter fluency)	57	8.8	10.5	19.3	<.001*	23.27	VAS	45	8.9	8.9	17.8
							NV	12	16.7	8.3	25
BADS Zoo Map	41	51.2	36.6	87.8 †	n/a	n/a	VAS	34	41.2	50.0	91.2
							NV	7	14.3	57.1	71.4
FrSBe self rated total	35	9.1	36.4	45.5	n/a	n/a	VAS	25	37.5	12.5	50
							NV	10	33.3	0	33.3

NOTE. VAS = vascular, NV = non-vascular. Impaired/borderline criteria: borderline (-1.99≤z≤-1.5; scale scores 4-5; ≤7th percentile approx.), impaired (z≤-2.0; scale scores 1-3; ≤2nd percentile), except; VOSP Position Discrimination (borderline: raw score 18/20; impaired: raw score ≤17/20), FrSBe (borderline: 60≤T≤64; impaired: T≥65). For the WTAR, the score terminology is 'borderline' or 'extremely low'.

* significant (p≤.003) after the Holm method of correction for multiple comparisons was employed

† % scoring 23 or less for the MoCA brief cognitive screen; % in two lowest BADS categories, 'borderline' and 'impaired', of seven-point ordinal classification).

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Table S1: Online Supplement

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Cognitive Functioning: Comparison of Vascular (VAS) and Non-Vascular (NV) Aetiology Groups

Domain	Assessment	Score Type	Normative M (SD)	Aetiology	N	M	Median	SD	Min to Max
Estimated premorbid intellectual ability	WTAR Standard Score	ST	100 (15)	VAS	38	95.71	99.5	20.56	50 to 123
				NV	12	97.75	100	15.61	64 to 120
Overall cognitive functioning	MoCA	Raw	n/a †	VAS	49	22.41	23	3.99	9 to 30
				NV	9	25.56	26	2.96	19 to 29
	RBANS Total Index	ST	100 (15)	VAS	58	83.5	84.5	17.43	45 to 121
				NV	15	90.6	92	13.73	69 to 109
Reasoning	WAIS-IV Block Design	SCL	10 (3)	VAS	48	8.02	8	3.1	1 to 17
				NV	12	8.92	9	3.53	2 to 16
	WAIS-IV Similarities	SCL	10 (3)	VAS	48	8.13	8	2.89	1 to 15
				NV	12	8.17	8.5	3.07	4 to 13
	WAIS-IV Matrix Reasoning	SCL	10 (3)	VAS	44	8.11	8	2.98	2 to 15
				NV	12	9.17	8.5	3.79	4 to 15
Psychomotor speed	D-KEFS TMT condition 5 (motor speed)	SCL	10 (3)	VAS	32	7.72	8	3.25	1 to 12
				NV	10	7.7	9	3.02	1 to 11
Information processing	D-KEFS CWIT condition 1 (color naming)	SCL	10 (3)	VAS	40	8.1	8	2.45	3 to 15
				NV	12	8.67	9	2.81	3 to 13
	D-KEFS CWIT condition 2 (word reading)	SCL	10 (3)	VAS	40	9.28	10	2.49	1 to 13
				NV	12	9.33	8.5	2.61	6 to 13
	RBANS Coding	Z	0 (1)	VAS	58	-1.87	-1.83	1.44	-5.08 to 1.54
				NV	15	-1.23	-0.97	1.05	-3.06 to 0.28

	WAIS-IV Symbol Search	SCL	10 (3)	VAS	49	6.86	6	2.91	3 to 18
				NV	11	7.55	7	3.17	1 to 12
Attention	RBANS Digit Span	Z	0 (1)	VAS	60	0.16	0.18	1.16	-2.47 to 2.76
				NV	16	0.03	0.18	1.14	-1.88 to 1.46
	D-KEFS TMT condition 1 (visual scanning)	SCL	10 (3)	VAS	42	7.64	9	3.3	1 to 13
				NV	10	8.7	8	2	6 to 12
	D-KEFS TMT condition 2 (number sequencing)	SCL	10 (3)	VAS	43	6.72	8	4.14	1 to 14
				NV	11	8.91	9	1.87	6 to 12
	D-KEFS TMT condition 3 (letter sequencing)	SCL	10 (3)	VAS	42	6.6	8	3.99	1 to 14
				NV	11	7.64	9	3.75	1 to 12
	TEA Telephone Search	SCL	10 (3)	VAS	24	5.38	5.5	2.67	1 to 13
				NV	8	7.25	7.5	3.54	2 to 12
	TEA Telephone Search With Counting	SCL	10 (3)	VAS	24	9	8	4.36	4 to 15
				NV	8	9.5	9	3.63	3 to 15
Memory	RBANS List Learning	Z	0 (1)	VAS	60	-1.01	-0.96	1.24	-3.88 to 1.38
				NV	16	-0.8	-0.79	1.14	-2.87 to 0.77
	CVLT-II SF Free Recall T-Score (list)	T	50 (10)	VAS	44	44.02	46	12.12	18 to 66
				NV	12	48.33	52	11.19	20 to 60
	RBANS Immediate Story Memory	Z	0 (1)	VAS	60	-0.46	-0.11	1.59	-4.65 to 1.76
				NV	16	0.025	0.2	1.17	-1.84 to 1.49
	WMS-IV Logical Memory I (story)	SCL	10 (3)	VAS	48	8.02	8	3.91	1 to 15
				NV	11	8.27	8	5.27	1 to 16
	CVLT-II SF Short Delay Recall (list)	Z	0 (1)	VAS	42	-0.46	-0.5	1.38	-2.5 to 4
				NV	11	-0.18	-0.5	1.38	-2.5 to 2

	RBANS Delayed List Recall	Z	0 (1)	VAS	60	-0.89	-0.87	1.13	-2.86 to 0.95
				NV	16	-0.73	-0.837	1.37	-3.61 to 1.39
	CVLT-II SF Long Delay Recall (list) [b]	Z	0 (1)	VAS	42	-0.58	-0.5	1.06	-2.5 to 2
				NV	10	-0.75	-0.5	0.98	-2.5 to 0.5
	RBANS Delayed Story Recall	Z	0 (1)	VAS	60	-0.85	-0.5	1.41	-3.68 to 0.91
				NV	16	-0.35	-0.5	0.78	-2.27 to 0.9
	WMS-IV Logical Memory II (story)	SCL	10 (3)	VAS	48	7.71	8	3.89	1 to 14
				NV	11	7.55	6	5.01	1 to 16
	RBANS Figure Recall	Z	0 (1)	VAS	62	-0.6	-0.7	1.07	-2.58 to 1.97
				NV	15	-0.16	-0.03	1.53	-3.48 to 1.67
	CVLT-II SF Long Delay Cued Recall	Z	0 (1)	VAS	42	-0.94	-0.75	1.07	-3 to 1
				NV	10	-0.65	-0.5	1	-3 to 0.5
	RBANS List Recognition	Z	0 (1)	VAS	60	-1.91	-1.17	2.36	-9.5 to 0.67
				NV	16	-2.66	0.16	6.44	-25.43 to 0.5
Language	RBANS Picture Naming	Z	0 (1)	VAS	60	-0.46	0.57	1.88	-7.4 to 0.9
				NV	16	-0.21	0.55	1.13	-2.29 to 1
	GNT raw score	Raw	n/a [†]	VAS	30	16.63	17.5	6.61	3 to 27
				NV	9	16.44	18	6.23	3 to 24
Visuospatial cognition	RBANS Figure Copy	Z	0 (1)	VAS	62	-1.35	-1.4	2.08	-8 to 1.29
				NV	15	-0.13	0.5	1.64	-5.21 to 1.29
	RBANS Line Orientation	Z	0 (1)	VAS	61	-0.54	-0.207	1.75	-5.5 to 4.62
				NV	16	0.72	0.73	0.866	-0.85 to 3.2
	VOSP Position Discrimination raw	Raw	n/a [†]	VAS	34	18.82	19.5	1.73	12 to 20
				NV	9	19.56	20	0.88	18 to 20
Executive functions	WAIS-IV Digit Span	SCL	10 (3)	VAS	50	9.38	9.5	3.17	2 to 17
				NV	12	10.08	11	3.4	3 to 15
	D-KEFS CWIT condition 3 (colour-	SCL	10 (3)	VAS	39	6.31	6	3.9	1 to 13

word switching)								
			NV	11	9.45	10	3.21	1 to 13
D-KEFS TMT condition 4 (number-letter switching)	SCL	10 (3)	VAS	42	5.38	5	3.83	1 to 13
			NV	11	7.45	9	4.34	1 to 13
RBANS Semantic Fluency	Z	0 (1)	VAS	60	-0.84	-0.87	1.22	-3 to 2
			NV	16	-1.38	-1.37	1.6	-5.8 to 0.38
D-KEFS VFT condition 1 (category fluency)	SCL	10 (3)	VAS	45	8.38	8	3.94	3 to 17
			NV	12	8.58	8.5	3.03	3 to 13
D-KEFS VFT condition 2 (letter fluency)	SCL	10 (3)	VAS	45	8.44	8	3.84	2 to 19
			NV	12	6.92	7.5	3.15	2 to 12
BADS Zoo Map	Raw	n/a †	VAS	34	n/a	2	n/a	1 to 6
			NV	7	n/a	2	n/a	1 to 6
FrSBe self rated total	T	50 (10)	VAS	25	61.04	59	17.27	29 to 99
			NV	10	56.7	53.5	15.42	35 to 82

† Raw scores: MoCA and GNT each have a possible raw scores ranging from 0 to 30. VOSP possible scores range from 0–20 (pass≥19, pass borderline=18, fail/impaired≤17/20). BADS zoo map possible scores range from 1 to 7 (pro-rated ordinal scale).

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