



RESEARCH ARTICLE

Post-stroke cognition with the Oxford Cognitive Screen vs Montreal Cognitive Assessment: a multi-site randomized controlled study (OCS-CARE) [version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract

Background: Cognitive impairment is common following stroke. The Oxford Cognitive Screen (OCS) was designed to assess focal post-stroke cognitive deficits in five domains. Here, we investigated whether results generated by the OCS vs the domain-general Montreal Cognitive Assessment (MoCA) at baseline impacted patient outcomes at 6 months follow-up.

Methods: Patients <2 months post-stroke were randomized to receive either the OCS and corresponding information leaflet or standard care with the MoCA at baseline. After 6 months, patients received both the OCS and MoCA. The primary registered outcome measures were the Stroke Impact Scale (SIS) and change in stroke severity (National Institutes of Health Stroke Scale; NIHSS) at 6 months. The secondary outcome was change in cognitive performance from baseline to 6-month follow-up. The relationship between scores from the two cognitive screens at follow-up was also explored.

Results: A total of 821 patients from 37 different hospital or rehabilitation sites (England, UK) were recruited to the OCS-CARE study, with 467 completing 6-month follow-up. Patient outcomes defined by overall SIS scores and changes in NIHSS did not differ between the OCS or MoCA groups. There were high concordance rates between the OCS and MoCA at 6 months, with severity of cognitive impairment reflected in both screening tools. Cognitive performance in both groups over the 6-month follow-up declined in 22% of patients. A larger proportion of OCS group patients demonstrated improvements in cognitive scores (49% vs 40% in MoCA).

Conclusions: The type of cognitive screening test did not impact broad stroke outcome measures, and the two screening tools showed a high overall concordance. The results suggest that more of the domain-specific deficits in OCS recover subacutely, providing a more granular picture of cognitive recovery as well as decline.

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Keywords

Stroke, Cognition, Post-stroke cognitive impairment, Cognitive assessment, OCS, MoCA

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Lay summary

Stroke survivors commonly experience difficulties with various aspects of thinking, planning and remembering, as well as seeing and speaking. These are often less obvious than physical problems, but are important to identify early after stroke in order to help guide rehabilitation and other treatment services.

In this study we randomly allocated 821 stroke survivors to one of two groups shortly after their stroke: one group received a cognitive assessment (Oxford Cognitive Screen) that assesses specific problems a patient may have after stroke, or another group that received a broader measure that assesses overall thinking performance (Montreal Cognitive Assessment). We then followed-up with them 6 months later to find out how they were recovering from their stroke. We collected data using a broad stroke severity measure that assesses a variety of abilities, such as the use of both arms and legs, etc. We also asked the patient to fill out a questionnaire regarding their own physical abilities, mood, communication, activities of daily life, participation in daily living, etc.

The aim of the study was to investigate whether the information provided by a cognitive screen regarding the specific cognitive problems experienced by the patient after stroke would lead to improved outcomes 6 months later. We found that the use of a cognitive screen right after stroke did not affect overall stroke recovery. We also found the cognitive screens to be in accordance with one another, in that people who struggle with one are also likely to struggle with the other. Despite not finding differences between patient outcomes between the two groups at follow-up, we did find that in the group that received the more specific cognitive screen after stroke, a higher proportion of people showed improvements than in the broad screening group. We believe this is because some of the stroke specific problems are recovering well over time. Further research into understanding what makes a person more likely to regain particular abilities is needed.

Introduction

Cognitive impairment is a common consequence of stroke. Studies reporting the prevalence of early post-stroke cognitive impairments suggest most patients experience at least one cognitive domain deficit (Demeyere *et al.*, 2015; Jaillard *et al.*, 2009). However, exact prevalence estimates of post-stroke cognitive impairment vary substantially in the literature depending on the nature and timing of the assessments being performed, as well as the methods of patient selection (Hurford *et al.*, 2013; Nys *et al.*, 2007). Still, post-stroke cognitive impairments are known to be a major determinant of poor long-term outcome and high societal costs in regards to increased mortality and disability rates (Hakkennes *et al.*, 2011; Patel *et al.*, 2002), functional outcomes and developing mood-related disorders (Nys *et al.*, 2005; Nys *et al.*, 2006).

Despite agreement that overall cognitive impairment is common after stroke, the co-occurrences and patterns of domain-specific deficits are not well understood. Cognition is often referred to as a single entity, with a binary description of

“impaired” or “non-impaired”. However, post-stroke cognitive impairment is complex, and does not constitute a unitary syndrome, with significant variability in stroke lesion location and size impacting on the nature and extent of the cognitive impairments such as executive functions, memory, language and visuo-spatial abilities (Jokinen *et al.*, 2015). Domain-specific cognitive screening targeting common post-stroke impairments, such as aphasia, apraxia, and hemi-spatial neglect, allows for a more comprehensive assessment of the specific problems and the relationships between them. This domain-specific approach is recommended in several clinical guidelines, including the UK National Institute for Clinical Excellence (NICE) guideline for stroke care (NICE, 2013), which specifically stated the need to assess performance across different domains of cognition after stroke (“attention, memory, spatial awareness, apraxia, perception”), and the RCP Clinical Guidelines for stroke (Rudd *et al.*, 2016), which suggested that “Each cognitive domain (e.g. perception, attention, memory) should not be considered in isolation because most everyday activities draw on a range of abilities.”

Due to the time limitations and resource constraints in acute stroke units, lengthy neuropsychological batteries for cognitive screening in the acute setting are impractical and unfeasible. Additionally, a large proportion of stroke patients experience quite severe impairments acutely and therefore are unable to participate in extensive cognitive assessments. Currently, most cognitive screening post-stroke mirrors that of an initial dementia test, with the use of broad measures such as the Mini-Mental State Exam (MMSE) (Folstein *et al.*, 1975) and the Montreal Cognitive Assessment (MoCA) (Nasreddine *et al.*, 2005). These two measures are the most commonly used cognitive screening instruments in stroke (Burton & Tyson, 2015; Pendlebury *et al.*, 2010), though they are not stroke-specific and the tasks assume certain intact cognitive functions, such as reading, writing, motor planning and vision. This is because these cognitive functions are generally unimpaired in patients with dementia, for whom the screens were traditionally designed (Kosgallana *et al.*, 2019; Mancuso *et al.*, 2018). Consequently, the use of the MMSE and MoCA in post-stroke screening can lead to common post-stroke impairments, such as aphasia and hemi-spatial neglect, contaminating patients’ performance on these dementia-based cognitive screening tasks (Demeyere *et al.* 2016; Mancuso *et al.*, 2018; Pasi *et al.* 2013).

The Oxford Cognitive Screen (OCS) (Demeyere *et al.*, 2015) was designed specifically for an acute stroke population with a neuropsychological foundation that provides a domain-specific cognitive profile. The OCS is structured around five domains: attention and executive function, language, memory, number processing and praxis. It takes approximately 15 minutes to complete, which is a similar testing length to the MoCA. The OCS was designed to be maximally inclusive as it is suitable for patients with aphasia and hemi-spatial neglect, and can be delivered at the bedside. Rather than an overall pass/fail score, the OCS provides a “visual snapshot” (Figure 1) of the cognitive profile to communicate, at a glance, areas of strengths and weaknesses for the specific cognitive domains. The OCS has

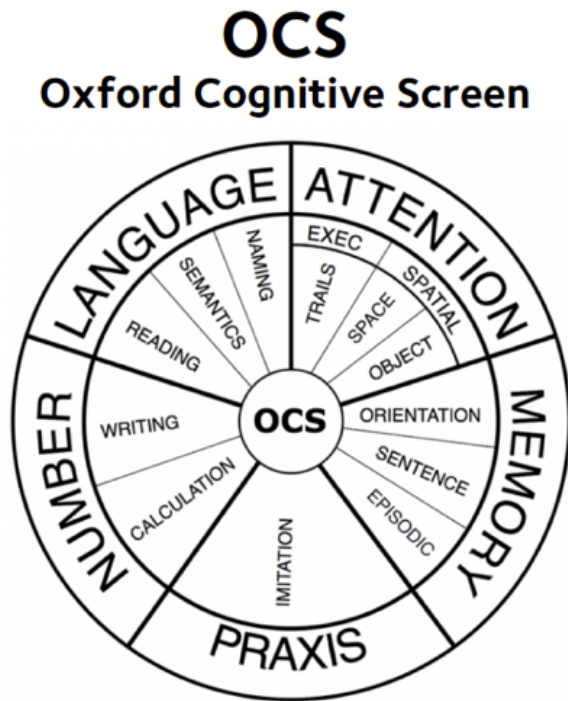


Figure 1. The Oxford Cognitive Screen (OCS) returns a visual snapshot of the patient's domain-specific cognitive profile.

recently been shown to be more sensitive than the MoCA (Demeyere *et al.*, 2016) and MMSE (Mancuso *et al.*, 2018) in detecting post-stroke cognitive impairment in (sub)acute stroke survivors.

Utilizing domain-specific cognitive screening and subsequently reporting results to the multidisciplinary team and patients/carers early in the rehabilitation pathway may impact outcomes. Detecting specific domain impairments may lead to improved rehabilitation, and more appropriate therapies that consider the particular limitations in cognition. Additionally, providing domain-specific information on possible coping strategies via information leaflets selected based on patients' cognitive screen results may lead to higher levels of adjustment. Therefore, the primary aim of this study was to investigate whether domain-specific screening early in the care pathway impacted long-term outcome.

The secondary aim of the study was to determine the trajectories for domain-specific post-stroke cognitive impairments over 6 months. Many studies have reported long-term post-stroke cognitive impairment may be attributable to the emergence of post-stroke and vascular dementia (Pendlebury *et al.*, 2015; Pendlebury *et al.*, 2019). This may be true for global impairment, but it is less clear whether stroke-related domain-specific impairments can improve, remain stable or decline over a long period of time (Del Ser *et al.*, 2005). Individuals may

experience several different domain impairments and collectively be classed as having 'post-stroke dementia' clinically, but when considering each domain impairment independently, there may be varying recovery trajectories. For example, many stroke survivors may present with a stable cognitive impairment over time, or indeed recover from various early focal deficits, such as hemispatial neglect (Demeyere & Gillebert, 2019). This would suggest that not all long-term post-stroke impairments are eligible for dementia consideration and equally, declining impairment in chronic stroke cannot exclude the contribution of vascular and age-related pathology. Thus, we examined the changes in cognitive performance from baseline to 6-month follow-up for the two screening groups with the aim of better characterizing differing cognitive trajectories.

Here, we report data from OCS-CARE, a multi-centre, randomized controlled study that investigated whether the results generated by the OCS and corresponding patient information leaflets versus results from the MoCA impacted long-term post-stroke outcomes. At 6 months post-stroke, participants completed both the OCS and MoCA, allowing us for the first time to compare domain-specific (OCS) and domain-general (MoCA) impairment levels for stroke survivors beyond the acute phase, and in relation to the baseline cognitive profiles. Here we compare proportions of patients whose cognitive performance declined, remained stable or improved over the first 6 months post-stroke.

Methods

Trial design

In this noninferiority randomized controlled study, sub-acute stroke patients were assigned at a 1:1 allocation ratio to either (a) cognitive profiling with the domain-specific Oxford Cognitive Screen (OCS) and tailored management advice or (b) standard care domain-general cognitive screening with the Montreal Cognitive Screen (MoCA) within 10 weeks following stroke. In all patients, overall stroke severity was documented via the National Institute of Health Stroke Scale (NIHSS) and impact on daily life was assessed via the Barthel Index of Activities of Daily Living (Barthel Index) (Mahoney & Barthel, 1965). After 6 months, outcome was evaluated via the Stroke Impact Scale (SIS) (Duncan *et al.*, 1999) and NIHSS, and all patients were assessed with both the OCS and MoCA. The trial was pre-registered at the ISRCTN Registry (ISRCTN50857950). The preregistration covered a broader research study and included additional further outcome measures on mood (Hospital Anxiety and Depression Score) (Zigmond & Snaith, 1983), activities of daily living (Nottingham Extended ADL) (Nouri & Lincoln, 1987), quality of life measures (ICECAP) and the Carer Strain Index. Because these measures are not relevant for the pre-registered primary and secondary outcome measures, they are not included in this paper.

Participants

Between July 2014 and July 2016, we recruited a consecutive sample of 821 acute stroke patients from 37 sites in England, UK (Table 1 and Figure 2). Patients were included if they met the following criteria: (i) acute stroke patient (within 10 weeks

Table 1. Number of participants per recruitment site.

Recruitment site	Participants (n)
The University Hospitals of North Midlands	122
Sandwell And West Birmingham Hospital Trust	97
St George's Healthcare NHS Trust	64
Cambridge University Hospitals NHS Trust	54
Shrewsbury And Telford Hospital	47
Sheffield Teaching Hospitals NHS Trust	38
Walsall Healthcare NHS Trust	38
Somerset Partnership NHS Foundation Trust	34
University Hospital Birmingham	33
Wye Valley NHS Trust	25
The Dudley Group of Hospitals	24
Plymouth Hospitals NHS Trust	23
The Royal Wolverhampton Hospital	21
Southend University Hospital NHS Trust	20
Staffordshire And Stoke-On-Trent Partnership NHS Trust	16
Guy's and St Thomas' NHS Foundation Trust	14
Ashford And St Peter's Hospitals Trust	13
Royal Cornwall Hospitals NHS Trust	13
East Kent Hospitals University Trust	11
Pennine Care NHS Foundation Trust	9
Weston Area Health NHS Trust	9
Peterborough And Stamford Hospitals Trust	7
Dorset County Hospital NHS Foundation Trust	7
Salisbury NHS Foundation Trust	7
Solent NHS Trust	7
University Hospital of South Manchester NHS Foundation Trust	7
Burton Hospitals NHS Foundation	6
Portsmouth Hospitals NHS Trust	6
Heart of England NHS Foundation	5
Norfolk Community Health and Care NHS Trust	4
Royal Hampshire County Hospital	3
Salford Royal NHS Foundation Trust	3
University College London Hospitals Trust	3
Royal Devon And Exeter NHS Foundation Trust	2
The Queen Elizabeth Hospital, King's Lynn NHS Foundation Trust	2
The Royal Liverpool And Broadgreen University Hospitals	1
York Teaching Hospital NHS Foundation Trust	1



Figure 2. Map with geographical locations of recruitment sites. The size of the circles indicates the number of participants recruited at the site.

of confirmed stroke); (ii) adult (≤ 90 years of age); (iii) able to concentrate sufficiently for one hour as judged by the multidisciplinary care team in the hospital; (iv) have sufficient language comprehension to pass the first orienting tests (the OCS Picture Naming and Semantics tasks); and (v) willing and able to give informed consent themselves. Patients were excluded if they were too unwell to take part, more than 10 weeks post-stroke, or had insufficient language comprehension to pass the first orienting tests in the OCS. All included participants provided written informed consent. All procedures were in accordance with the Declaration of Helsinki and approved by the West Midlands – Coventry and Warwickshire National Research Ethical Committee (REC reference 12/WM/00335).

Cognitive screening groups

Patients allocated to the OCS screening group received a cognitive assessment with the OCS and were given the corresponding

information leaflets on management of domain-specific cognitive impairments (available as *Extended data*; Demeyere *et al.*, 2019c). The OCS is a stroke-specific cognitive screen (normative data, validation, reliability and sensitivity measures of the OCS reported previously in Demeyere *et al.* (2015)) and is freely available for non-commercial use at <http://www.ocs-test.org>. The test provides 14 subtest scores that can be categorized into five domains: (1) attention and executive function, (2) language, (3) memory, (4) number processing and (5) praxis. The OCS takes approximately 20 minutes to complete and was administered to participants by a UK Clinical Research Network research facilitator or an occupational therapist at the acute stroke ward. The number of failed subtests were recorded (cut-off scores also reported previously in Demeyere *et al.* (2015)) and a patient was considered to be impaired in a certain domain if they failed any of the subtests of that domain. Patients would receive a single-page leaflet for each of the five

domains they show an impairment in (available as *Extended data*; Demeyere *et al.*, 2019c). Each leaflet explained the common impairments in that domain, (e.g. unilateral neglect, sustained attention and executive dysfunctions pertaining to the attention domain) alongside coping strategies and therapeutic exercises for the patient and family/carer to refer to.

Participants assigned to the MoCA group completed the Montreal Cognitive Assessment (MoCA), which is a freely available cognitive screen that consists of a single A4 page. Though the MoCA contains assessments of several cognitive functions, they are typically not marked separately, resulting in a single overall cognitive score. A score <26 out of 30 is considered indicative of cognitive impairment (Nasreddine *et al.*, 2005). The MoCA takes approximately 15 minutes to complete and was administered to participants by a UK Clinical Research Network research facilitator or an occupational therapist at the acute stroke ward.

Outcomes

A UK Clinical Research Network research facilitator or a member of the clinical care team completed both the NIHSS and the Barthel Index for all participants acutely (≤ 10 weeks post-stroke). The NIHSS is a brief 11-item questionnaire that addresses cognitive and motor problems after stroke. Questions pertain to motor ability (e.g. eye gaze), sensory deficits (e.g. visual field tests), as well as the presence of aphasia and neglect. The NIHSS has reliable validity for clinical research and predictive validity for long-term stroke outcome, with four categories: very severe: >25 ; severe: 15–24; mild-to-moderately severe: 5–14; and mild: 1–5 (Brott *et al.*, 1989). The Barthel Index consists of 10 items that measure a person's daily functioning, specifically the activities of daily living and mobility. The items include feeding, moving from wheelchair to bed and return, grooming, transferring to and from a toilet, bathing, walking on level surface, going up and down stairs, dressing, and continence of bowels and bladder. At 6 months follow-up, the Stroke Impact Scale (SIS) was administered and the OCS, MoCA, NIHSS and Barthel Index were repeated for all participants. The SIS is a questionnaire containing 59 items that cover 8 dimensions, providing a composite disability score that characterizes disability and health-related quality of life after stroke. The follow-up assessment was performed at the original site or at an additional research visit by the UK Clinical Research Network research facilitators.

Sample size

Recognizing substantial attrition in previous studies (including death, morbidity and other loss to follow-up) (Barbay *et al.*, 2018; Pendlebury *et al.*, 2015), we estimated a follow-up cohort of 50% of our initially recruited sample. The sample size calculations indicated that recruitment of 736 patients with 368 included in follow-up would allow for the detection of a Cohen's d effect size of 0.30 with power 0.8 and at 5% significance level. This Cohen's d effect size reflects a difference in SIS scores of 3 points between both screening groups with an expected standard deviation of 10 in each group.

Randomization

Individual acute stroke patients were allocated to either the OCS or MoCA screening by a computer randomization service at all 37 sites. We obtained a balanced randomization over all sites by using block randomization with a block size of 4. The randomization sequence was concealed from all researchers until assignment. A participant was enrolled in the study by the UK Clinical Research Network research facilitators who logged on to the project website and obtain the next available randomization code and assigned the participant to either the OCS or MoCA screening group.

Blinding

Participants, test administrators, care providers and data-analysts could not be blinded during the study.

Data analysis

Pre-specified analysis included descriptive statistics for demographics, reasons for loss to follow-up and clinical characteristics of each group (frequencies, mean and standard deviations). We quantified severity of cognitive impairment by the number of subtests on which a patient scored below the cut-off score for the OCS and by the total score for the MoCA. Patients were classified as impaired if they failed ≥ 1 subtest on the OCS or had a MoCA score of <26 . When comparing MoCA scores over time (baseline to follow-up), a difference of ≥ 2 points must be observed in order to be considered clinically significant. This operationalized criterion was previously demonstrated by Tan *et al.* (2017).

For our primary analyses, we report the distributions of scores on the cognitive tests and outcome measures. From the initial assessment, we compared severity between both groups, as reflected in the NIHSS and Barthel Index, with Wilcoxon rank sum tests to account for skewness in the data. Linear regression was performed to evaluate the association between severity and cognitive impairment at the acute stage. At follow-up, we evaluated the mean difference between each group's NIHSS and SIS scores with a Wilcoxon Mann-Whitney Rank-Sum test with continuity correction due to the scores for both groups being not normally distributed. Assessing the change in NIHSS scores from the acute assessment to 6 months was carried out by a Welch two-sample t test, as the scores were approximately normally distributed.

Our secondary analyses compared improvement in cognition on either the OCS or MoCA in both groups by calculating the difference in scores at the acute and follow-up assessment in a Bland-Altman analysis. We also calculated the percentage of patients who improved, declined or remained stable in each group and then compared proportional distributions between both groups with a χ^2 test. Lastly, we explored the relationship between the OCS and MoCA results at follow-up through a linear regression. All statistical testing was performed at a two-sided 5% significance level. Analyses were completed using R software version 1.1.383 (2017). The full analysis code is available on Figshare (Demeyere *et al.*, 2019a), along with the *Underlying data* (Demeyere *et al.*, 2019b).

Results

A total of 821 acute stroke patients were randomly assigned to either the OCS screening group (n=411) or the standard care screening group with the MoCA (n=410). Upon further investigation, 6 patients that were initially randomized did not meet inclusion criteria and were therefore excluded. Additionally, 19 patients were withdrawn from the study before completing baseline assessment (deteriorating condition or voluntary withdrawal). The randomized sample size for analysis at baseline assessment was n=399 (OCS group) and n=397 (MoCA group).

A total of 467 patients completed a follow-up visit, with loss-to-follow-up being attributed to study withdrawal (n=95),

unable to be contacted (n=98), incomplete assessment (n=71), death (n=29) and 27 patients were undocumented loss-to-follow-up. The CONSORT flow-diagram summarizes the patient pathway in [Figure 3](#) and patient demographics at baseline are shown in [Table 2](#).

Cognitive screening at baseline

At baseline, 75% of patients who received the OCS were impaired in ≥ 1 cognitive domain and 58.37% of patients in the MoCA group were cognitively impaired based on a score < 26 . The distributions of the scores in both groups was skewed ([Figure 4](#)), with more patients in the sample who had fewer cognitive impairments, represented by a low score on the OCS and a high score on MoCA.

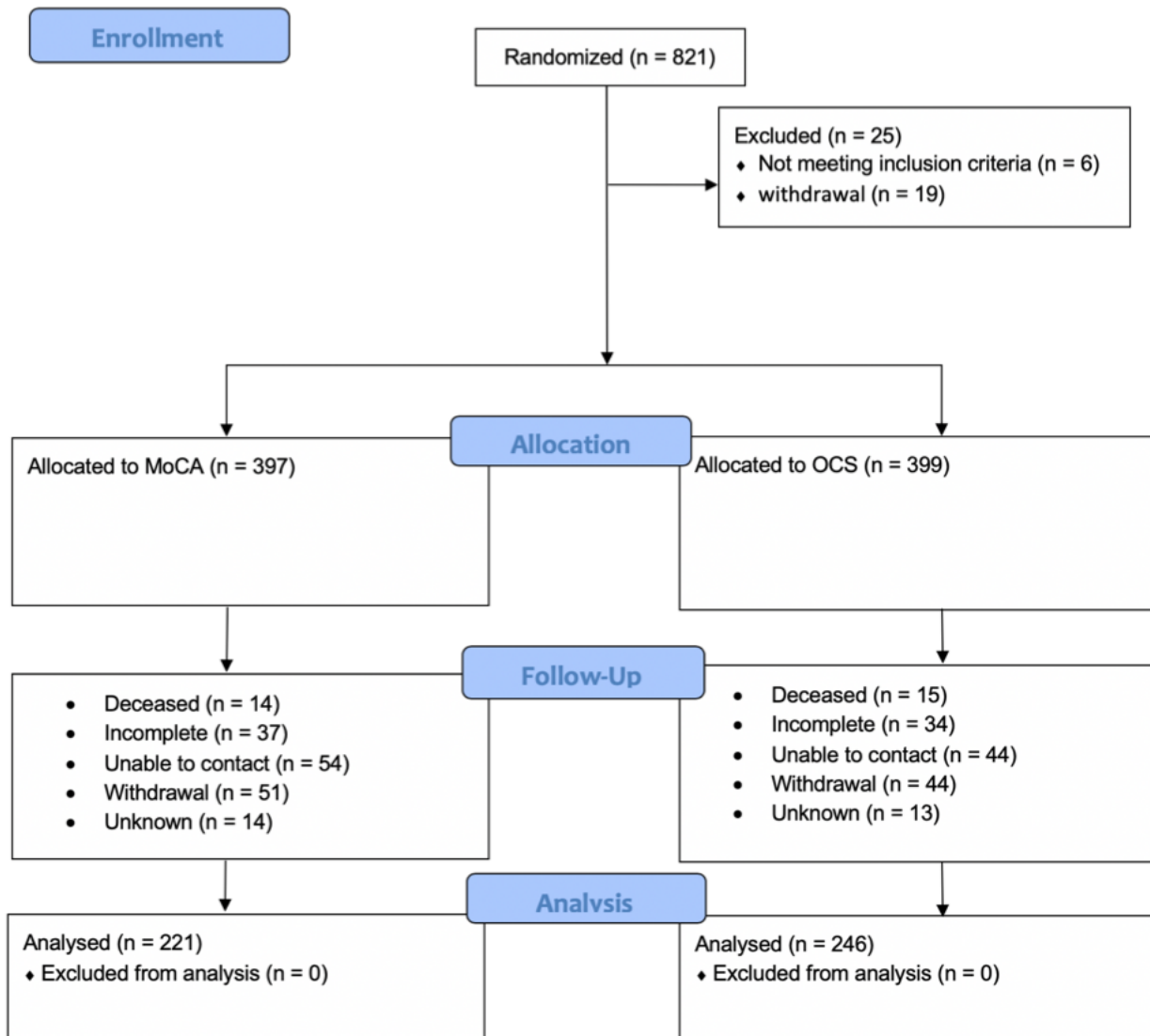


Figure 3. CONSORT flow-diagram of participants.

Table 2. Baseline demographics.

Characteristic	Participants initially allocated (n=796)				Participants completed follow-up (n=467)			
	MoCA		OCS		MoCA		OCS	
	N	%	N	%	N	%	N	%
Age (years), mean(SD)	69.0(12.29)		69.0(12.78)		69.1(12.06)		69.7(12.24)	
Gender								
Male	214	53.9	219	54.9	117	52.9	126	51.2
Female	183	46.1	180	45.1	104	47.1	120	48.8
Years of education, mean(SD)	11.6(3.77)		11.8(3.57)		12.1(4.24)		11.8(3.01)	
Days since stroke, mean(SD)	13.4(15.26)		14.2(15.47)		13.4(15.96)		14.7(15.89)	
Type of stroke								
Ischemic	282	71.0	288	72.2	156	70.6	184	74.8
Hemorrhagic	43	10.8	48	12.0	21	9.5	28	11.4
TIA	3	0.8	0	0.0	2	0.9	0	0.0
Other	6	1.5	7	1.8	4	1.8	5	2.0
Unknown	63	15.9	56	14.0	35	15.8	29	11.8
Stroke side								
Right hemisphere	152	38.3	100	25.1	86	38.9	63	25.6
Left hemisphere	99	24.9	109	27.3	48	21.7	59	24.0
Bilateral	11	2.8	18	4.5	7	3.2	12	4.9
Unknown	135	34.0	172	43.1	80	36.2	112	45.5
Trial completion								
Complete	221	55.7	246	61.7	221	100.0	246	100.0
Withdrawal	51	12.8	44	11.0				
Unable to contact	54	13.6	44	11.0				
Incomplete	37	9.3	34	8.5				
Deceased	14	3.5	15	3.8				
Unknown	14	3.5	15	3.8				

Stroke severity at baseline (NIHSS and Barthel Index) was compared between groups (Figure 5). Wilcoxon rank sum tests indicated no significant differences between the two groups (NIHSS: $n = 464$, Hodges Lehmann estimator = 0, 95% CIs = [0,1], $W = 28215$, $p = 0.34$, $d = -0.06$; Barthel Index: $n = 452$, Hodges Lehmann estimator = 0, 95% CIs = [0,0], $W = 24813$, $p = 0.61$, $d = 0.09$). Within each group, we did observe a relationship between stroke severity and cognitive impairment (Figure 6); patients who were impaired on more subtests on the OCS had a higher NIHSS score (reflecting a more severe stroke) (estimated slope = 0.26, 95% CIs = [0.19,0.32], R-squared = 0.2, $t(240)=7.66$, $p < 0.0001$), while a lower score on MoCA was associated with a higher NIHSS score (estimated slope = -0.38, 95% CIs = [-0.55,-0.21], R-squared = 0.08, $t(219) = -4.43$, $p < 0.0001$). Conversely, we observed more severe cognitive impairment in those who had lower Barthel Index scores (OCS: estimated slope = 0.15, 95% CIs = [-0.2,-0.11], R-squared = 0.18, $t(230) = -7.16$,

$p < 0.0001$; MoCA; estimated slope = 0.31, 95% CIs = [0.2,0.43], R-squared = 0.11, $t(216) = 5.24$, $p < 0.0001$).

Primary outcome at 6 months follow-up

No reliable difference between the OCS and MoCA groups was found on the Stroke Impact Scale (Wilcoxon rank sum test, $n = 459$, Hodges Lehmann estimator = -1.5, 95% CIs = [-3.5,0.25], $W = 23854$, $p = 0.09$, $d = 0.18$, Figure 7A). NIHSS scores at 6 months follow-up also did not differ between groups (Wilcoxon rank sum test, $n = 466$, Hodges Lehmann estimator = 0, 95% CIs = [0,0], $W = 29370.5$, $p = 0.09$, $d = -0.1$, Figure 7B), as well as change in NIHSS scores between baseline and 6 months post-stroke (Wilcoxon rank sum test, $n = 463$, Hodges Lehmann estimator = 0, 95% CIs = [0,0], $W = 26680$, $p = 0.97$, $d = -0.01$, Figure 7C). This indicates that patients had a similar outcome regardless of which cognitive screen they received.

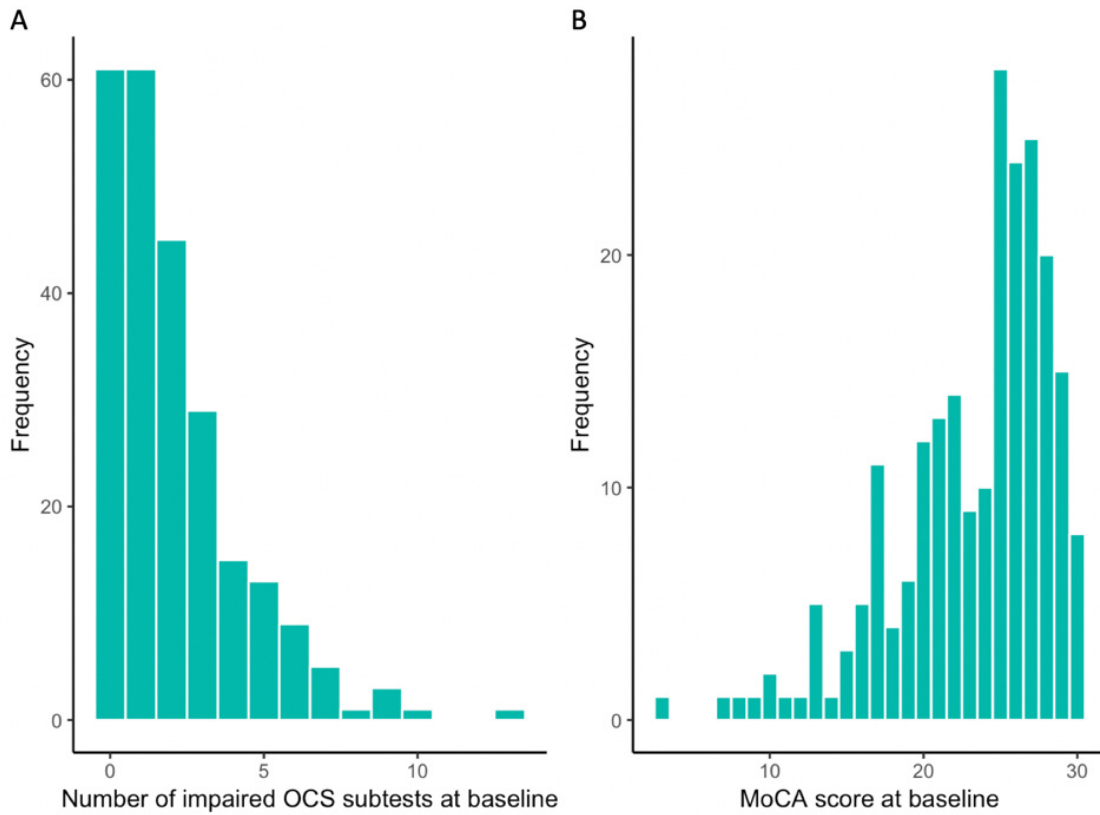


Figure 4. Histograms of baseline scores. (A) Histogram of number of impaired subtests on Oxford Cognitive Screen (OCS) at baseline. (B) Histogram of scores on Montreal Cognitive Assessment (MoCA) at baseline.

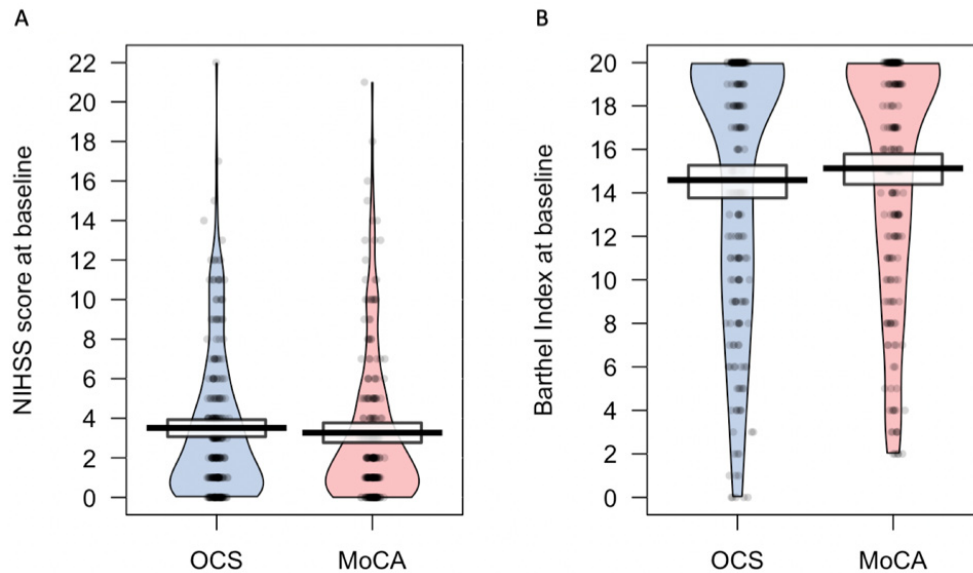


Figure 5. Distribution of severity scores at baseline for both screening groups. (A) National Institutes of Health Stroke Scale (NIHSS) and (B) Barthel Index. The dots indicate individual data points, the thick horizontal line represents the mean, the lower and upper edge of the box show the boundaries of 95% Bayesian Highest Density Intervals (HDI) of the mean, and the shaded area indicates the density.

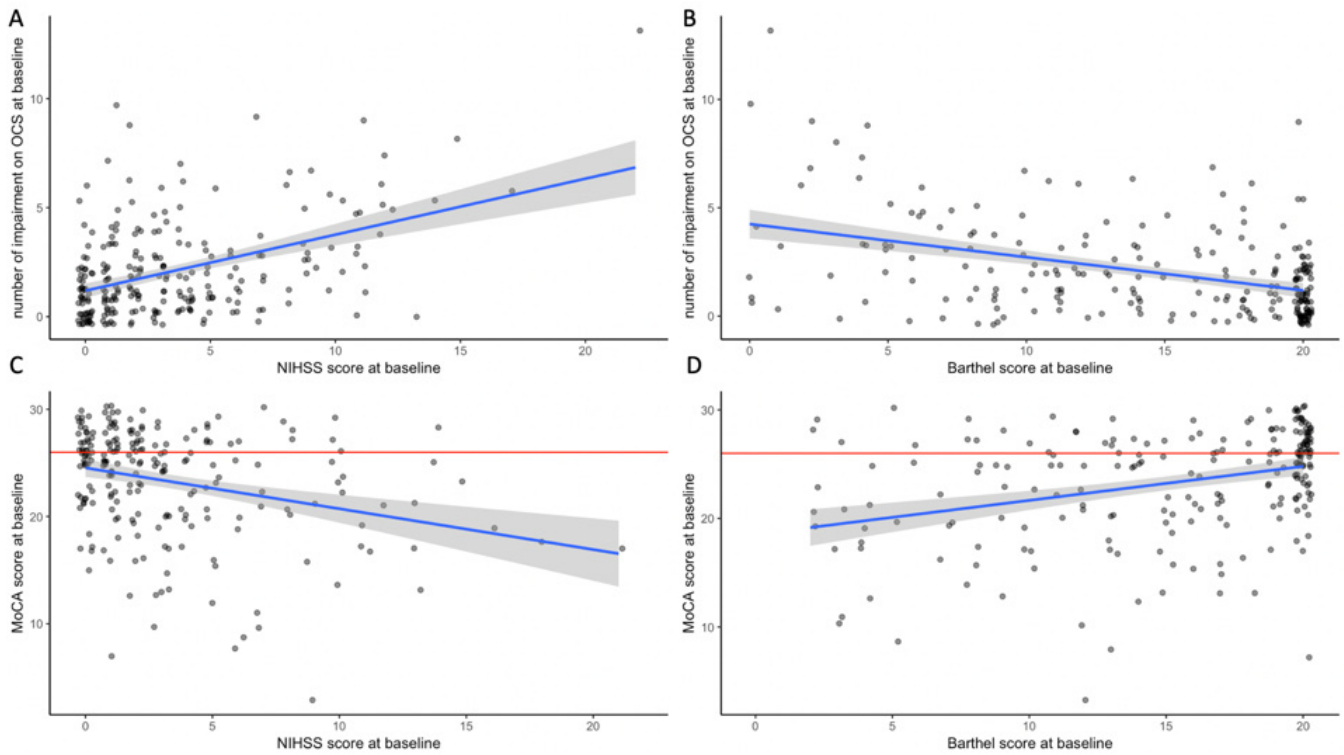


Figure 6. Comparison of the different scoring systems. Scatter plots of (A) Oxford Cognitive Screen (OCS) versus National Institutes of Health Stroke Scale (NIHSS) scores, (B) OCS versus Barthel Index scores, (C) Montreal Cognitive Assessment (MoCA) versus NIHSS scores, and (D) MoCA versus Barthel Index scores, each with a regression line. The horizontal line represents the cut-off score of 26 on the MoCA. The shaded areas around the regression line show the 95% confidence level interval for predictions from a linear model.

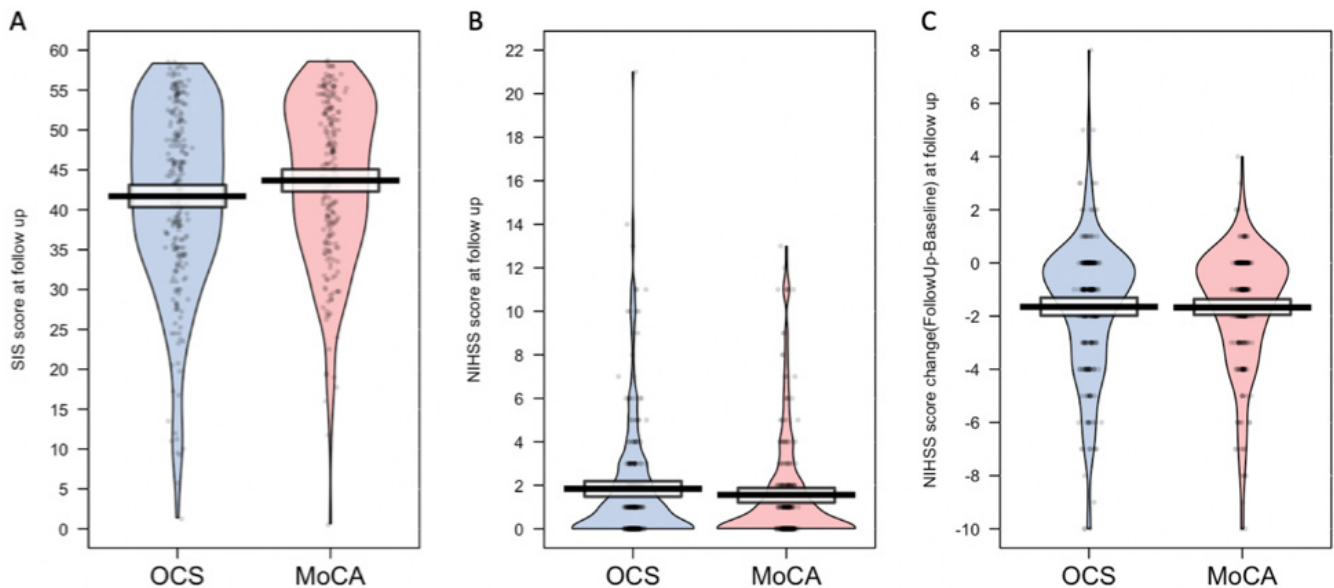


Figure 7. Scores at 6 months post-stroke. Distribution of (A) SIS scores 6 months post-stroke, (B) National Institutes of Health Stroke Scale (NIHSS) scores 6 months post-stroke, and (C) changes in NIHSS scores between baseline and 6 months post-stroke for each group.

Secondary outcome at 6-months follow-up

Cognitive status at 6-months follow-up was compared between the two groups. Patients in the MoCA group, overall as a group, showed a small, but insignificant trend for decline in cognition (Bland-Altman analysis, $n = 218$, mean difference = -1.408 with 95% CIs = $[-1.918, -0.898]$, Lower LOA = -8.896 , Upper LOA = 6.079 , [Figure 8A](#)) that did not vary with average MoCA score. Within the OCS group, we did not observe a systematic change in cognition, regardless of their average performance (Bland-Altman analysis, $n = 243$, mean difference = 0.597 with 95% CIs = $[0.359, 0.834]$, Lower LOA = -3.091 , Upper LOA = 4.284 , [Figure 8B](#)).

In addition to examining the average improvement in cognitive function, we compared the proportion of patients who showed an improvement, decline or no change in cognition at 6 months. Within the OCS group, 49% of patients showed an improvement, while 22% declined and 29% remained stable. In regards to the MoCA group, we defined improvement and decline as a difference of ≥ 2 points on the overall score ([Krishnan et al., 2016](#); [Tan et al., 2017](#)); 40% of patients showed improvement, whereas 22% declined and 38% remained stable. A Pearson's χ^2 test indicated these proportional distributions were significantly different from each other ($\chi^2 = 39.61$, $df = 2$, $p < 0.0001$, Cramer's V = 0.29).

Lastly, the relationship between scores on the OCS and the MoCA at 6 months was explored. A total of 467 patients completed both the OCS and MoCA at follow-up ([Figure 9](#)). A significant

relationship was found between both cognitive screens (linear regression: estimated slope = -1.71 , 95% CIs = $[-1.86, -1.56]$, R-squared = 0.52, $t(460) = -22.31$, $p < 0.0001$, kappa = 0.372), suggesting agreement between both tests. Patients showed the same pattern regardless of whether they were assessed with OCS or MoCA at baseline ([Figure 9A](#) versus [9B](#)). [Figure 10](#) explores the relationship between MoCA scores and impairments on each of the five domains in the OCS. Qualitatively, the data indicates that the most common impairments in our sample at 6–8 months post stroke, are in the attention and memory domains. Furthermore, the data suggests there is no association between overall MoCA score and any specific OCS domain, confirming the MoCA as a domain-general measure.

Discussion

The OCS-CARE study set out to investigate cognitive outcomes at 6 months based on domain-specific versus domain general cognitive screening within 10 weeks of stroke. By 'domain-specific' we refer to problems in a particular process that contributes only to the domain in question – for example, a deficit in spatial orienting affecting spatial attention but not (say) language comprehension. By 'domain-general' we refer to a process that supports a variety of cognitive domains, such as working memory and sustained attention, which support language, memory, number processing etc. Collectively, these impairments may impact recovery differently, e.g. regarding focal cognitive impairments, hemi-spatial neglect may recover while overall cognition may still decline, leading to post-stroke dementia.

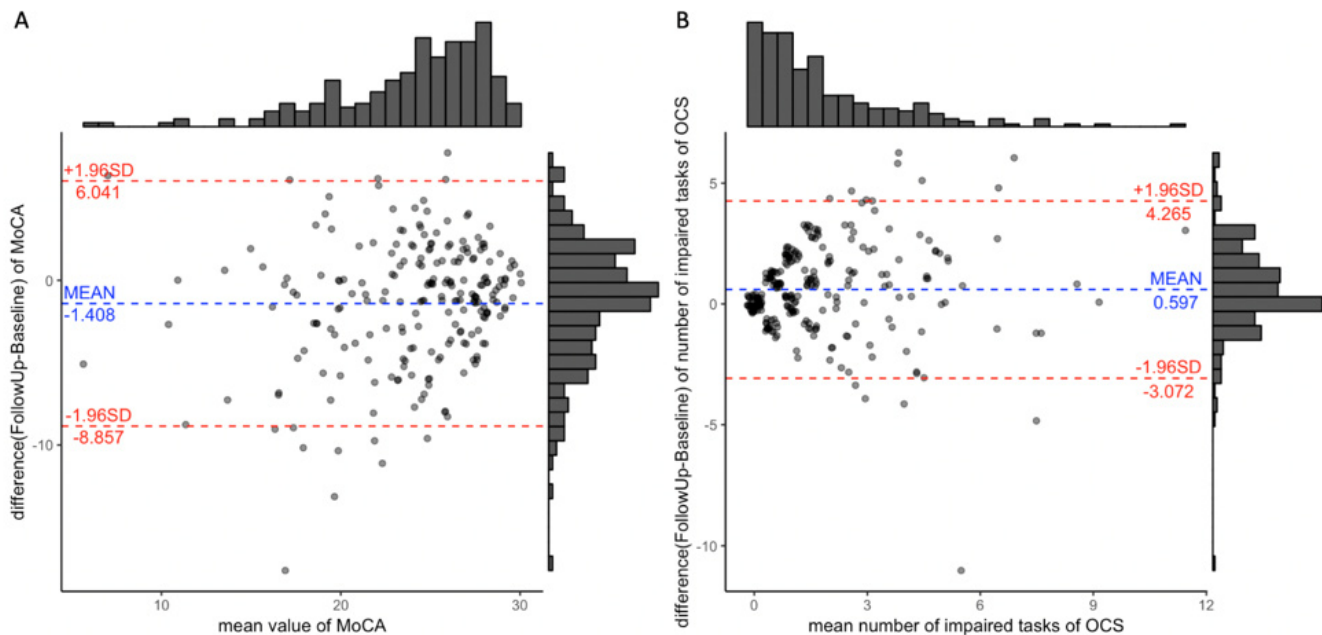


Figure 8. Changes in scores at 6 months follow-up. (A) Bland-Altman plot of change in Montreal Cognitive Assessment (MoCA) scores from baseline to follow-up at 6 months. (B) Bland-Altman plot of change in number of impaired Oxford Cognitive Screen (OCS) subtests from baseline to follow-up at 6 months. The middle blue horizontal line represents the average difference between both measures. The upper and lower red horizontal lines show Limits of Agreement. We show the distributions of average (top) and differences (right) in scores on the sides of the Bland-Altman plots.

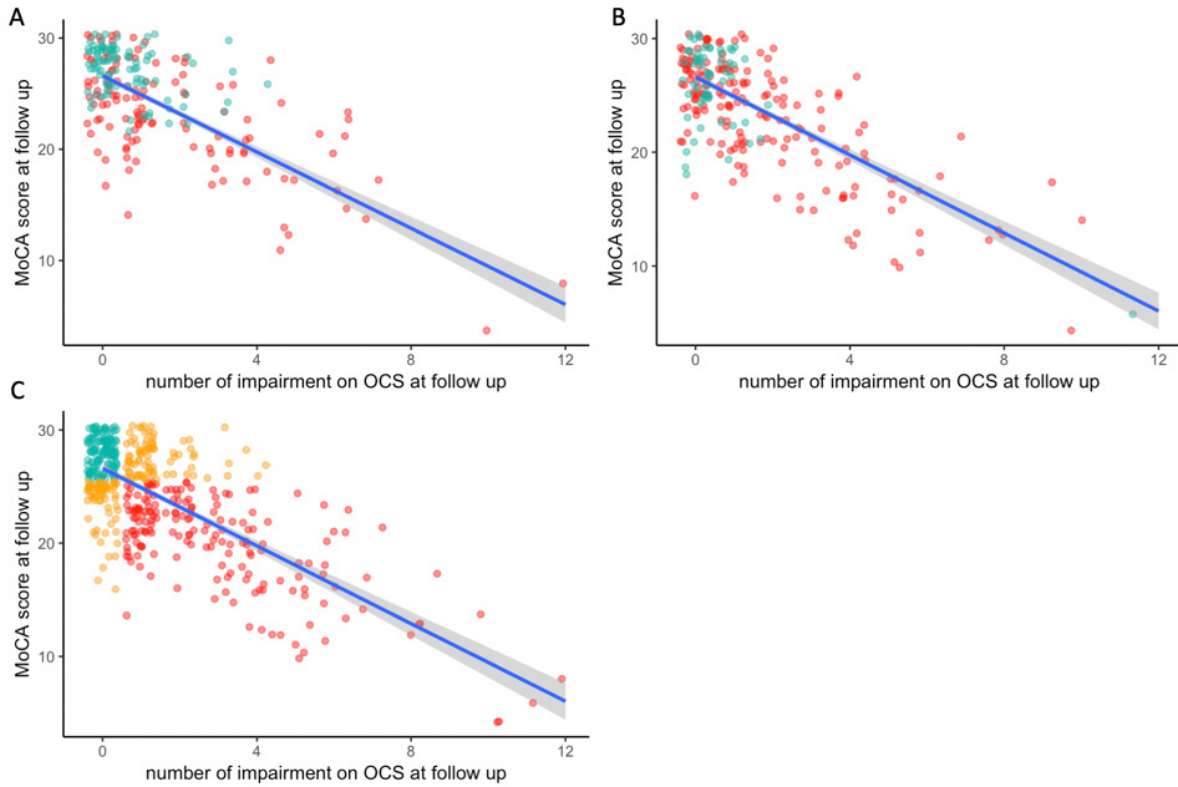


Figure 9. Scatter plots of Montreal Cognitive Assessment (MoCA) versus Oxford Cognitive Screen (OCS) scores at 6-month post-stroke. (A) Patients in the standard care group receiving MoCA, (B) Patients in the intervention group receiving OCS and information leaflets. (C) All patients where green data points indicate patients for whom both OCS and MoCA agreed that they did not have a cognitive impairment (MoCA ≥ 26 and OCS < 1 failed subtest). Red data points indicate patients for whom both OCS and MoCA agreed that they have a cognitive impairment. Amber data points indicate a disagreement between OCS and MoCA.

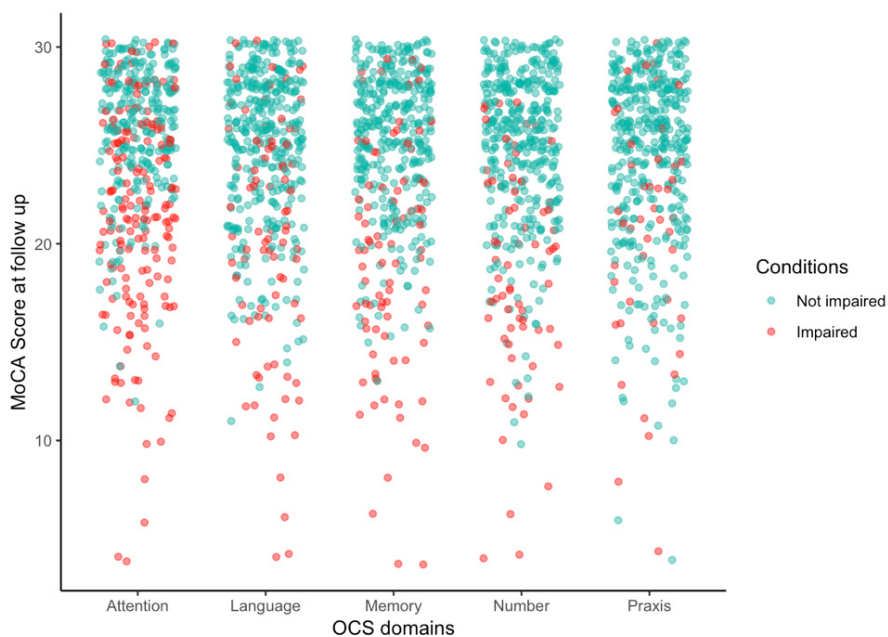


Figure 10. Jittered scatterplot of Montreal Cognitive Assessment (MoCA) scores for each of the Oxford Cognitive Screen (OCS) domains. Patients who are impaired on a certain OCS domain are plotted in red for that domain, unimpaired patients are plotted in green. This is an interactive plot: by clicking on the legend you can show or hide each category. You can zoom in by holding the mouse button down and dragging a square around the area you want to zoom in on. Hovering the mouse over the data points will show the data values. The online version of this figure is interactive.

A total of 821 patients were randomised to either cognitive screening with the OCS or MoCA, and followed-up with functional outcome and cognitive measures after 6 months at 37 sites in England, UK. The initial sample consisted of 54% males, with an overall average age of 69 years and 11.8 years of education. Given the national average of 72 years for first-ever stroke ([Public Health England, 2018](#)) and this inclusive sample also recruiting recurrent stroke survivors, this cohort would appear to be slightly younger than would have been expected. The distribution of stroke severity scores (NIHSS median (IQR): 2 (1–5) at baseline in this population were also lower than previously reported studies ([Abdul-Rahim *et al.* \(2015\)](#): n=6483, NIHSS median (IQR) 12 (8–17); [Reznik *et al.* \(2018\)](#): NIHSS median (IQR) 8 (3–17)). In addition, the skewed distributions suggest that there was a slight bias in the multi-site recruitment to this research towards younger and less severely impaired stroke survivors. Nevertheless, even in this perhaps overall milder stroke sample, cognitive impairment was highly prevalent both at baseline and follow-up. At baseline, 75% of patients demonstrated at least one cognitive domain impairment in the OCS group and 58% of patients were impaired in the MoCA group (below standard MoCA cut-off). A reliable relationship between severity of cognitive impairment and stroke severity was found in both screening groups of the study, where patients who scored higher on the NIHSS demonstrated more extensive cognitive impairments. Similarly, a relationship was found between the severity of cognitive scores and lower Barthel scores.

In regards to comparing stroke severity and impact outcomes at 6 months follow-up, no difference in the core outcome measure of Stroke Impact Scale scores or NIHSS was found, demonstrating no difference in global outcome for domain-specific vs domain-general cognitive screening.

There are a few significant limitations regarding the study design. First, no information was recorded regarding potentially differing care pathways that may have been followed given a particular cognitive profile. Though the researchers were asked to provide leaflets to patients and carers, as well as report findings in the medical notes, it is not clear whether and to which extent these cognitive reports were considered. It is likely that the 33 different settings differed in their approaches here. These differences could be due to differences in established care pathways, routine treatments, familiarity with the screening tools etc. Finally, the approaches would likely also differ depending on how many patients were recruited at the sites (with some sites only recruiting a small number of patients). Second, differences related to more specific psychological outcomes could be missed and not included in such broad functional outcome measures such as the stroke impact scale and NIHSS. A more tailored and extended measure on cognitive coping might provide a more sensitive outcome measure here. Third, we suggest that a stronger understanding of cognitive care pathways might be better achieved with randomising settings where one pathway is consistently followed, and documented in depth, rather than the present design of randomising at the individual patient level.

With regards to the secondary outcome measures that were confined to cognitive changes, we found no systematic overall improvement or decline over the 6 months in either the MoCA or OCS group. Instead, the findings demonstrated that within this heterogeneous cohort, a proportion of patients improved (49% OCS; 40% MoCA group), a proportion remained stable (29% OCS; 38% MoCA) and a proportion of patients declined (22% in both groups), cancelling out a systematic effect. We found no relationship between the severity of initial cognitive impairment and the likelihood of improvement vs decline in overall cognition in either group. However, when assessing the differing proportions, it appeared that a larger proportion of patients who were assessed with OCS demonstrated improvements (49%) compared to the proportion of patients improving on MoCA (40%). These findings are reminiscent of the heterogeneous cognitive trajectories found in a longer term follow-up study by [Del Ser *et al.* \(2005\)](#). At 2 years post stroke, they found cognitive status to be stable in most cases (78%), some patients demonstrating cognitive decline and (14%) and 8% improved (total N=49). Here, we found much larger proportions of recovery, both with OCS and with MoCA. However, the timelines were different (earlier follow-up), and the cognitive status measure in [Del Ser *et al.* \(2005\)](#) is likely to be less sensitive to small levels of change.

In addition to differences in sensitivity of cognitive measures, in our study, the difference in proportions of recovery is likely to also reflect the difference in the aspects of cognition that are being measured. Specifically, the improvements may reflect recovery of stroke-specific impairments, such as reading impairments, hemi-spatial neglect and apraxia. These will likely have led to improved scores on both OCS and MoCA measures, though we suggest that the increased rates of improvement on the OCS may be driven by a more explicit measure of these focal cognitive deficits.

It is important to note that the aetiology of long-term cognitive deficits is not necessarily related to a progressive neural degeneration; following stroke, cognitive evolution beyond the acute phase of recovery is indeed heterogeneous, as many patients may remain stable or even improve over time ([Del Ser *et al.*, 2005](#)). However, many large-scale studies consider cognitive impairments on a single score, and thereby reduce the complexity of neuropsychological understanding. When using measures borrowed from the field of dementia, it is important to note that this can lead to confounded results, where people with aphasia are excluded or fail on tasks due to language impairments ([Demeyere *et al.*, 2016](#); [Mancuso *et al.*, 2018](#)). Large-scale monitoring studies have highlighted the importance of cognition in assessing outcomes, but improved measures to understand the contributing factors are needed. When time permits, cognition should be assessed in more detail, particularly long after stroke in order to determine changes over time.

Finally, when directly comparing performance on the MoCA and OCS at follow-up where both tests were completed, we found a clear agreement between both tests, with highly related levels of scores on both and no difference for the two

screening groups in the study. Further exploration of the data revealed that there was no association between MoCA scores and any one specific OCS domain, indicating that the MoCA appears to be measuring a global level of functioning in the chronic stage following stroke.

In conclusion, this randomised study found no difference in global outcome measures whether OCS or MoCA was completed as the first step of a cognitive care pathway post stroke. The study demonstrated high agreement rates between the cognitive screening measures, a clear relation between severity of stroke and severity of cognitive impairments and importantly highlighted longer-term cognitive outcomes to be highly heterogeneous, with cognitive trajectories 6 months post stroke demonstrating large proportions of stability and improvements along with approximately a fifth of patients following a declining cognitive trajectory.

Data availability

Underlying data

Figshare: Post-stroke cognition with the Oxford Cognitive Screen vs Montreal Cognitive Assessment: a multi-site randomized controlled study (OCS-CARE) Dataset. <https://doi.org/10.6084/m9.figshare.9199541.v2> (Demeyere *et al.*, 2019b).

This project contains the de-identified underlying data collected in this study.

Extended data

Figshare: Post-stroke cognition with the Oxford Cognitive Screen versus Montreal Cognitive Assessment: a multi-site randomized controlled study (OCS-CARE). Information leaflets. <https://doi.org/10.6084/m9.figshare.9250568.v1> (Demeyere *et al.*, 2019c).

This project contains the information leaflets given to participants enrolled in the study.

Reporting guidelines

Figshare: CONSORT checklist for article 'Post-stroke cognition with the Oxford Cognitive Screen versus Montreal Cognitive Assessment: a multi-site randomized controlled study (OCS-CARE)'. <https://doi.org/10.6084/m9.figshare.9255653.v1> (Demeyere *et al.*, 2019d).

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/) (CC-BY 4.0).

Software availability

Analysis code used in this study available from: <https://doi.org/10.6084/m9.figshare.9199604.v2> (Demeyere *et al.*, 2019a).

License: CC-BY 4.0.

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The authors present data from a noninferiority randomized controlled study examining the relationship between performance on the OCS/MoCA and stroke outcome measures (SIS and NIHSS) at baseline and at 6 month follow-up. The large multi-centre trial found no difference in stroke outcome (SIS or NIHSS score) based on the cognitive screening tool administered at baseline. Also, they found no systematic overall improvement or decline over 6 months in either the OCS or MoCA.

Comment:

The broad topic is interesting and important. However, it remains uncertain why the authors think using a particular type of screen might alter the overall functional impact of a stroke at 6 months. They should specifically explain why they hypothesise this could happen. For example, do they think that an improved screen might lead to uncovering deficits to guide rehabilitation input after stroke?

Introduction:

As above to explain the motivation of the study, more discussion is needed as to why the authors might expect the administration of a cognitive screen to change stroke outcome scores on functional/neurological measures such as the NIHSS and Barthel. Is there any previous research to support the author's hypothesis? On the face of it, the result seems to be fully expected and unsurprising, unless the assessment battery is linked to a specific intervention. Can the authors please clarify and comment?

More clarity is needed to differentiate the role of domain-specific assessment versus the giving of domain-specific feedback and strategies to the patient. Perhaps the authors believe both aspects are important, but this needs to be made clearer and consistent throughout the manuscript.

The study of domain-specific impairment after stroke, its relevance to long-term outcome and the trajectory of recovery over time is not new. The authors should make greater effort to include findings from past studies in both the introduction and discussion for completeness and transparency.

(for example: Nys, G. M. S., Van Zandvoort, M. J. E., De Kort, P. L. M., Van der Worp, H. B., Jansen, B. P. W., Algra, A., ... & Kappelle, L. J. (2005). The prognostic value of domain-specific cognitive abilities in acute first-ever stroke¹.

Hurford, R., Charidimou, A., Fox, Z., Cipolotti, L., & Werring, D. J. (2013). Domain-specific trends in cognitive impairment after acute ischaemic stroke².

Zietemann, V., Georgakis, M. K., Dondaine, T., Müller, C., Mendyk, A. M., Kopczak, A., ... & Dichgans, M. (2018). Early MoCA predicts long-term cognitive and functional outcome and mortality after stroke³)

Methods:

How and by whom was the leaflet regarding strategies delivered to the patient? Was any additional input provided to patients? Did the patients in the MoCA group get any feedback?

Results:

Can the authors comment on selection bias? Over two years recruitment at 21 NHS stroke units one would have expected at least 200 patients per site (conservatively) meaning there would have been well over 8000 eligible patients over this period. Can the authors comment on what proportion of patients potentially eligible were actually included (e.g. from NIHR screening logs). Alternatively can they see how their cohort compares to an unselected UK database, e.g. SSNAP? Specifically some measure of stroke severity at baseline (e.g. NIHSS) would be helpful. This is crucial to understand the generalisability of the findings. Can the authors please provide these data?

Please report the mean timing and range of the assessments at baseline and 6 months for the two groups.

Primary outcome – For completeness, it would be interesting to see whether the results differ for the different SIS/NIHSS subscales. At present, the authors only present on overall score.

Secondary outcome – Given that the authors argue for the importance of understanding domain-specific impairment after stroke, it is surprising that the analyses does not take into account domain-specific change over time. It would be interesting to see whether there are different trajectories for the different domains as suggested by previous studies (e.g. Hurford, R., Charidimou, A., Fox, Z., Cipolotti, L., & Werring, D. J. (2013). Domain-specific trends in cognitive impairment after acute ischaemic stroke²).

The authors look at the relationship between MoCA overall score and OCS domains and find no significant association. However, the MoCA does examine different domains (even though they might not be validated). It may be more fair/meaningful to compare performance on MoCA domain subtests with OCS domains as has been done in other studies (e.g. Chan, E., Khan, S., Oliver, R., Gill, S. K., Werring, D. J., & Cipolotti, L. (2014). Underestimation of cognitive impairments by the Montreal Cognitive Assessment (MoCA) in an acute stroke unit population⁴.

Discussion:

The authors' definition of Domain-general in the first paragraph is somewhat confusing. Although the MoCA produces an overall score, it would not be accurate to suggest that this score reflects a 'domain-general' cognitive process as described by the authors. As the authors pointed out, the MoCA was designed to detect dementia. The issue here is that the MoCA treats cognition as a unitary concept with a one score outcome. I would avoid suggesting that the MoCA assesses a fluid intelligence-like processes as there is no basis for this.

The authors should discuss the possible impact of premorbid cognitive status on the trajectory of recovery

after stroke.

Thank you for interesting work.

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Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Stroke, cerebral small vessel disease, cognition, intracerebral haemorrhage.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Reviewer Report 10 October 2019

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The authors present data from a multi-site non-inferiority RCT evaluating the effect of cognitive screening post-stroke using either the Montreal Cognitive Assessment (MoCA) or the Oxford Cognitive Screen (OCS) on patient outcomes at 6-month follow up. They found no differences in stroke severity or stroke impact.

This is a very timely piece of research, given the recent monetisation of the MoCA and its implications.

I suggest the following minor changes:

Introduction:

p 3 - The authors state the OCS takes 15 mins to complete in the introduction but later in the methods section (p6), it says the OCS takes 20 minutes to complete.

Methods – Trial Design: p4 – Pre-registration also included measures of anxiety and depression, quality of life, activities of daily living, and carer strain. If the authors are planning an additional paper looking at these measures, they should include the citation (even if manuscript in preparation). Otherwise, please report descriptives from these measures in supplemental materials as this will be of great interest to other researchers.

Methods – Participants: p6 – it is evident from the inclusion criteria that those with severe cognitive impairment/dementia were excluded from the trial. I would state this explicitly.

Methods – Participants: p6 – were the inclusion criteria the same for carers? Please supply their demographic details as well (in supplemental materials or citation to manuscript in preparation).

Methods – Participants: p6-7 – UK Clinical Research Network research facilitators and OTs administers the screening assessment on the stroke ward. It would be of benefit to readers outside of the UK to explain a bit more about whom these research facilitators are, their role in research, training etc.

Methods – Participants: p6-7 – Did the UK Clinical Research Network research facilitators receive specific training on how to administer and interpret the OCS/MoCA?

Methods – Participants: p6-7 – Did the UK Clinical Research Network research facilitators/ OTs go through the tailored management advice sheet with each patient or give it to them to read in their own time? – ties in to fidelity of intervention delivery.

Methods – Outcomes: p7 – How long did the follow up testing session take?

Methods – Outcomes: p7 – Did follow up occur 6 months post-stroke or 6 months post initial baseline assessment? It would be useful to include Mean (SD) weeks since stroke based on timing of the follow-up assessment also.

Results: p8 – for context, it would be useful to the reader (particularly those outside the UK) to have a brief description of what measures are usually taken post-stroke in the acute setting as part of standard care, e.g. are all patients screened for cognitive impairment post-stroke or is this done on an ad hoc basis/ varies across sites?

Results – baseline demographics: p9 – suggest including another column describing the baseline characteristics of those lost to follow up. It would be interesting to see if they were older, more severely impaired (cognitively), had recurrent stroke etc.

Results – baseline demographics: p9 – how many participants across groups had recurrent stroke?

Results: p12 – suggest changing wording in second paragraph from average “improvement” to average “change” in cognitive function (to encompass improvement, decline, and no difference).

Results: p12 – it would be really interesting if the authors reported on the domain-specific cognitive impairments identified at 6-months by the OCS and if specific domains showed change from baseline to follow-up as measured by the OCS.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: stroke; cognitive rehabilitation; cognitive assessment

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
