Title:

The test accuracy of the Montreal Cognitive Assessment (MoCA) by stroke lateralisation

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Abstract

Background: The Montreal Cognitive Assessment (MoCA) is an increasingly popular screening tool for detecting cognitive impairment post-stroke. However its' test accuracy by stroke lateralisation is as yet unknown.

Aim: Our aim was to investigate whether the test accuracy of the MoCA differs by stroke lateralisation across different cognitive domains.

Methods: We retrospectively examined the cognitive profiles of 228 subacute stroke patients (86 Left, 142 Right), comparing MoCA-total and domain-specific scores with performance on detailed neuropsychological assessment.

Results: The prevalence of cognitive impairment detected on neuropsychological assessment was high and relatively comparable between the right and left hemisphere stroke groups (91% and 93% respectively). Notably however, 29% of the right stroke group and 6% of the left stroke group achieved a "cognitively-intact" MoCA score (≥ 25). A high proportion of right stroke patients who had an overall MoCA-intact score were found to be impaired in intellectual functioning, processing speed, executive functions and non-verbal memory on neuropsychological assessment. Furthermore, a high proportion of patients who scored full-marks within a MoCA-specified domain, irrespective of their overall score, were found to have impairment on corresponding neuropsychological assessment for both stroke groups.

Conclusions: Particular care needs to be taken in interpreting MoCA-intact performance for right hemisphere patients due to its poor sensitivity to right hemisphere deficits. Scoring maximum points within a MoCA-specified domain also does not necessarily indicate intact cognitive functioning in that domain. Clinicians should consider supplementing their MoCA assessment with additional tools to increase the test accuracy of detecting relevant cognitive impairments post-stroke.

Keywords: cognition; stroke; Montreal Cognitive Assessment; neuropsychology; executive functions; lateralisation

1. Introduction

In acute stroke care, the accurate and early detection of cognitive impairment is used to inform rehabilitation and discharge planning. Stroke lateralisation can lead to different patterns of cognitive deficits with equally significant impact on functional outcomes (1–3). As such, detailed domain-specific cognitive assessments are recommended in the context of a multidisciplinary approach (4). However, brief screening measures are sometimes used for pragmatic reasons or deemed more clinically appropriate in patients with milder events or in those who are unable to tolerate longer complex assessments. Therefore, it is important that screening measures have the breadth and accuracy to detect post-stroke cognitive impairments in order to highlight any concerns that may warrant further investigations (5). Historically, the Mini Mental State Examination (MMSE) has been most commonly used (6). However, recent reviews have recommended the Montreal Cognitive Assessment, MoCA (7), for stroke-based cognitive screening (5,8,9), particularly in mild to moderate strokes without significant aphasia (10). The MoCA contains more test items assessing stroke-relevant domains and has been shown to have better sensitivity in detecting global impairment than the MMSE (11,12).

Few studies have directly compared performance on the MoCA to more detailed domain-specific neuropsychological assessment. Results so far are difficult to consolidate across studies because of variability in the case-mix, the timing of assessments and the way in which neuropsychological data was analysed. A study that assessed stroke patients at 1- or 5- year follow-up found comparable sensitivity and specificity for detecting amnestic impairments (13), whilst another study which assessed patients at a mean post-stroke interval of 24.1 days found good sensitivity but only moderate specificity for global impairments (14). Similarly, in a cohort of patients with chronic aneurysmal subarachnoid haemorrhage, the MoCA was shown to have better sensitivity than the MMSE but only moderate specificity (15,16). In a recent retrospective study examining patients with subacute ischaemic or haemorrhagic stroke, we found 77% of patients were impaired across one or more cognitive domains on neuropsychological assessment despite being classed as cognitively intact on the MoCA (17). Notably, the majority of patients with a MoCA-intact score (≥25) had right hemisphere strokes. This provides preliminary suggestion that the MoCA may have different test accuracy depending on stroke lateralisation. Although cognitive deficits following left hemisphere stroke such as aphasia can have an obvious impact on daily functioning, less obvious cognitive deficits following right hemisphere stroke can have an equally profound impact on long-term functional outcomes (1). Bias' against detecting deficits in patients with right hemisphere stroke compared with left hemisphere stroke have already been shown in other common stroke assessment scales such as the NIHSS (18,19). Under-detection of cognitive deficits following right hemisphere strokes may lead to inadequacies in rehabilitation and discharge planning or bias decisions or interpretation regarding research or treatment protocols.

Examination of the MoCA's test accuracy to stroke lateralisation has been limited. A study by Cumming and colleagues (20) examined the relationship between MoCA performance and cognitive impairment 3-months post-stroke. They found no difference in the mean MoCA

score between left and right hemisphere stroke patients. However, MoCA performance had greater predictive validity for global cognitive impairment for right hemisphere stroke patients compared with left hemisphere stroke patients. The authors argued that this was because the MoCA contained attention/visuospatial items that were more sensitive to right hemisphere stroke impairments. However, patients with significant language impairments were excluded from the study, likely biasing the sample. In contrast, a more recent study using a voxel-based lesion-symptom mapping (VLSM) found that poor MoCA performance at 3-months post-stroke was mainly associated with lesions in the left hemisphere (21). The authors suggested that perhaps left hemisphere strokes are more likely to result in poorer long-term cognitive outcome. Alternatively, it may be that the MoCA is more sensitive to detecting left hemisphere stroke impairments. Indeed, it has been shown that left hemisphere stroke patients are more likely to have difficulty completing, and score lower, on the MoCA compared with right hemisphere strokes, due to the high language demands of most MoCA subtests (22,23). Neuropsychological assessment data was not available in the study for comparison. As yet however, no study has investigated in detail whether the test accuracy of the MoCA in detecting cognitive impairment differs by stroke lateralisation, particularly across the different cognitive domains. Examination of possible lateralisation differences will help clinicians better understand and interpret MoCA findings. The aim of this study was to address this important question by comparing MoCA performance with performance on detailed neuropsychological assessment in a cohort of subacute stroke patients.

2. Method

A retrospective cohort study of patients admitted 24-72 hours post-stroke to the Acute Stroke/Brain Injury Unit, NHNN, between January 2011 and December 2014 was examined (n=469). Inclusion criteria were the availability of MoCA and neuropsychological data (n=262). Exclusion criteria were patients with bilateral strokes (n=25), comorbid substance misuse or severe psychiatric disorders (n=9). Demographic and clinical information collected comprised of sex, age, stroke type and lateralization. All patients were assessed on the MoCA followed by a tailored neuropsychological assessment by a Clinical Neuropsychologist who was blind to the aims of the current study as a part of standard routine care. Testing lasted approximately 60-90mins in total and was generally conducted in one session unless patients were too fatigued. The neuropsychological assessment evaluated seven cognitive domains: premorbid intellectual functioning, current intellectual functioning, memory, naming, perception, information processing speed and executive function. Premorbid intellectual functioning was assessed using the National Adult Reading Test (NART) (24). Current general intellectual functioning was assessed using the Wechsler Adult Intelligence Scale—Third Edition (WAIS-III) (25). Verbal and visual memory functions were assessed with either the Recognition Memory Test (26) or the Doors and People test (27). Naming skills were examined either with the Graded Naming Test (28) or the Oldfield Naming Test (29). Perceptual functions were assessed using the Visual Object and Space Perception Battery (30). Information processing speed was examined using one or more of the following tests: the 'O' Cancellation, Digit Copy (31), Symbol Digit Modalities Test (32) or Trail Making Test (Part A) (33). Executive functions were examined using one or more of the following

tests: the Stroop Test (34), Trail Making Test Part B (33), Weigl Colour Form Sorting Task (35) or Hayling and Brixton Test (36). Standardised test administration was employed. The results were scored using published normative data adjusting for age and education where applicable. Patients were classified as intact on the MoCA if they scored ≥25 out of 30. This cut-off was chosen as it has been shown to provide the optimal sensitivity and specificity for detecting cognitive impairment in a post-stroke sample (13). For neuropsychological assessments, performance at or below the 5th percentile on any one test were taken to indicate impairment in that respective domain. For intellectual functioning, impairment was classified as a difference of greater than 10 points between either the Verbal or Performance IQ measure of the Wechsler Adult Intelligence Scale – Third Edition and the respective premorbid functioning score on the National Adult Reading Test.

Two analyses were conducted. First we identified the cohort of patients obtaining MoCA ≥25 by stroke lateralisation and examined their performance on neuropsychological assessment. Secondly, we identified patients obtaining flawless scores on the individual MoCA domains (e.g. naming, memory), irrespective of their overall score, and examined their performance on corresponding neuropsychological assessments. We calculated the relevant positive predictive value (PPV) and negative predictive value (NPV); see for a similar methodology Chan et al. (17). Our study was approved by the local clinical governance and ethics committees using de-identified data collected as part of routine clinical practice.

3. Results

A total of two hundred and twenty-eight patients with a unilateral stroke were identified who had both MoCA and neuropsychological assessment data. Of those, 86 (38%) patients had a left hemisphere stroke and 142 (62%) had a right hemisphere stroke. There was no significant difference between the two stroke groups on age, sex, time since injury and assessment, type of stroke or estimated premorbid intellectual functioning (see Table 1). The right hemisphere stroke group had significantly lower performance IQ than the left hemisphere stroke group but there was no difference between the two groups on verbal IQ.

Table 1
Demographic and clinical characteristics by stroke lateralisation

	Left (n=86)	Right (n=142)	Left vs Right
Age in years (SD)	67.60 (14.45)	64.41 (14.49)	p = 0.11 [d]
Sex – male/female	55/31	76/66	p = 0.14 [e]
Days since injury (SD)	13.10 (20.52)	12.30 (15.52)	p = 0.74 [d]
Infarct/Haemorrhage	70/16	110/32	p = 0.48 [e]
Premorbid intellectual functioning NART (SD) [a]	104 (16.22)	106.65 (14.63)	p = 0.45 [d]
Current intellectual functioning Verbal IQ (SD)[b]	93.57 (19.24)	94.98 (17.09)	p = 0.80 [d]
Performance IQ (SD)[c]	95.8 (16.51)	84.66 (17.04)	**p = 0.07** [d]

a left, n = 29; right, n = 55.
b left, n = 14; right, n = 44.
c left , n = 10; right, n= 35.
d Independent samples t-test.
e Pearson Chi-square.

The prevalence of cognitive impairment identified on neuropsychological assessment was not significantly different between the two stroke groups, with 123 (91%) right hemisphere stroke patients and 75 (93%) left hemisphere stroke patients found to be impaired in at least 1 cognitive domain (Fisher's exact test, p>0.1), with a majority having impairments in 2 or more domains (84% and 92% respectively, Fisher's exact test, p>0.1). Overall, right hemisphere stroke patients were more likely to have visuoperceptual impairment (Fisher's exact test, p<0.01) whereas left hemisphere stroke patients were more likely to have naming impairment (Fisher's exact test, p<0.05). There was no significant difference between the two stroke groups in the likelihood of impairment in general intellectual functioning, information processing speed, verbal memory, non-verbal memory or executive functions (Fisher's exact test, p>0.1).

The right hemisphere stroke group scored significantly higher on the MoCA overall score compared with the left hemisphere stroke group (p<0.01). Strikingly, in our sample 41 patients (29%) in the right hemisphere stroke group had a MoCA-intact score (≥25) whereas only 5 patients (6%) in the left hemisphere stroke group had a MoCA-intact score. That is, patients with right hemisphere strokes were more likely to have MoCA-intact overall scores compared with left hemisphere strokes (Fisher's exact test, p<0.01). Importantly however, the proportion of impairment detected on neuropsychological assessment for the left and right hemisphere stroke groups was not significantly different as reported above. As such, at the recommended cut-off of ≥25 (13), the MoCA appears to have poorer sensitivity for patients with right hemisphere strokes compared with left hemisphere strokes. Specificity is poor for both groups but worse for patients with left hemisphere stroke. For both the left and right groups, the MoCA has good positive predictive value but very poor negative predictive value (see Table 2).

Table 2
MoCA performance characteristics by stroke lateralisation

	Left (n=86)	Right (n=142)
MoCA raw score (SD)	15.17 (6.89)	18.80 (7.38)
MoCA - % Intact (≥25)	6%	29%
MoCA - % Impaired (<25)	94%	71%
Sensitivity	0.94	0.72
Specificity	0.14	0.45
Positive Predictive Value	0.92	0.91
Negative Predictive Value	0.2	0.17

Importantly, a high proportion of the MoCA-intact population were found to have cognitive impairment on neuropsychological assessment both in the left and right hemisphere stroke group. For the left stroke group, 4 of the 5 patients (80%) with MoCA-intact scores were impaired on at least one cognitive domain on neuropsychological assessments with 2 patients impaired on two cognitive domains. For the right stroke group, 36 (88%) patients were impaired on at least one domain on neuropsychological assessments. Of the 36 patients, thirty (83%) were impaired on two or more domains while the remaining six (17%) were impaired in one cognitive domain only. Impairment in the right stroke group with MoCA-intact scores was most commonly found in intellectual functioning (63%), information processing speed (57%) and executive function (46%). A relatively high proportion of patients were also found to be impaired on non-verbal memory (31%) and visuo-perceptual/spatial difficulties (22%). Impairment in naming and verbal memory was less commonly detected (10% and 5% respectively).

We also compared the performance of patients who scored the maximum points within MoCA-specified domains, irrespective of their overall score, with their performance on corresponding neuropsychological tests. The percentage of patients who were found to have impairment is summarized in Table 3. Despite scoring full marks on the attention domain of the MoCA, greater than 50% of patients were found to have impairment on corresponding neuropsychological tests in both the left and right groups. A high percentage of patients were also found to have impairment on visuospatial/executive function, abstraction and naming. Notably, the proportion of patients found to have impairment on neuropsychological tests across the MoCA-specified domains were similar between the left and right groups (Fisher's exact test, p>0.1). In keeping with this, the negative predictive values (NPV) between the two groups for the different domains were comparable.

Table 3
Percentage of patients (no.) impaired on neuropsychological assessment by different MoCA-specified cognitive domains and the corresponding NPV.

MoCA-Specified domain	Left	NPV	Right	NPV
Attention	67% (6/9)	0.2	58% (15/26)	0.27
Visuospatial/Executive	40% (4/10)	0.55	43% (9/21)	0.57
Abstraction	33% (6/18)	0.4	34% (11/32)	0.31
Naming	26% (11/42)	0.65	21% (18/86)	0.72
Language	14% (1/7)	0.55	3% (1/29)	0.85
Memory	0 % (0/4)	1	1% (2/20)	0.86

4. Discussion

Our findings demonstrate that the MoCA has poorer test accuracy for detecting cognitive deficits in patients with right hemisphere strokes compared with left hemisphere strokes.

Right hemisphere stroke patients scored significantly better on the MoCA and were more likely to be classified as cognitively intact. However, a large proportion of the MoCA-intact right hemisphere stroke patients were found to have impairment in at least one cognitive domain on neuropsychological assessment.

Our current findings build upon our previous preliminary observation that a higher number of patients with right hemisphere stroke obtained intact scores on the MoCA compared with left hemisphere stroke (17). In this study, we were able to extend this preliminary observation in a much larger sample of patients. Importantly, we were able to demonstrate that the difference in sensitivity of the MoCA was not due to actual differences in the prevalence of cognitive impairment between the two stroke groups. The prevalence of cognitive impairment found on neuropsychological assessment was largely comparable between the two stroke groups. Moreover, for the first time, we were able to characterize the pattern of neuropsychological impairment that was associated with right hemisphere stroke patients who obtained an intact score on the MoCA. We found that a high proportion of patients had impairments in general intellectual functioning, information processing speed and non-verbal memory, three domains that are not assessed by the MoCA. Impairments in these areas are common following all stroke (37,38), but have been found to be particularly pertinent following right hemisphere strokes (39,40).

Notably, a large proportion of right hemisphere stroke patients with intact MoCA scores were also found to have impairment in executive functions, a domain that is assessed by the MoCA. Our findings suggest that although the MoCA has more items assessing executive functions than other screening tools such as the MMSE, it still has its' limitations. This is not surprising given that the construct of executive functions is likely complex. It is commonly thought to encompass multiple distinctive higher-order cognitive processes relating to specific frontal lobe regions. A brief screening measure is unlikely to capture all the facets adequately. Notably, at least one of the "executive" tasks on the MoCA (e.g. phonemic fluency) is known to rely mainly on left frontal brain regions (41–43) and therefore may not be as sensitive to detecting right hemisphere impairments.

Our findings also demonstrate that the MoCA has good sensitivity for detecting left hemisphere stroke impairments. Cumming and colleagues (20) argued that the MoCA had greater predictive validity for right compared with left hemisphere stroke patients. However, patients with significant language impairments were excluded in their study. This likely biased their sample to finding less left hemisphere impairments. In our study, only 5 of the 86 left hemisphere stroke patients achieved an intact score on the MoCA. The poor performance of left hemisphere stroke patients on the MoCA most likely reflect the demand of the MoCA subtests on both receptive and expressive language abilities as well as verbal working memory abilities, which are commonly affected following a left hemisphere stroke. Although our findings suggest the MoCA is effective in detecting gross impairment following left hemisphere stroke, the large language component to most of the subtests, even those that are not specifically testing language functions, may reduce the test accuracy of the MoCA for detecting domain specific impairments or indeed non-impairments (22). The large language

burden of the MoCA may reduce the clinical utility in detecting non-language based cognitive impairments for left hemisphere stroke patients.

When we examined performance within MoCA-specified domains, the negative predictive value was similarly poor between right and left hemisphere stroke patients. Consistent with our previous finding (17), scoring full marks on a MoCA-specified domain did not guarantee intact performance on neuropsychological assessment. Greater than half of the patients who scored full marks on the MoCA attention domain and a third of patients on the visuospatial/executive and abstraction domain were found to have impairments on comparable neuropsychological assessment for both the left and right hemisphere stroke patients. This again highlights the notion that the prevalence of high-level cognitive impairments following stroke are somewhat independent of neuroanatomical location (3). The development of appropriate measures to adequately capture likely impairment irrespective of stroke location is clinically important. Identification of domain-specific cognitive impairment has been shown to be good predictors of length of stay, long-term rehabilitation needs and functional outcomes (44,45).

It is worth noting that we used a cut-off of <25 to define impairment on the MoCA, in keeping with optimal sensitivity and specificity found in a previous post-stroke UK sample (13). Other studies, however, have recommended lower cut-off scores in a French (14) and Chinese population (16). Whether laterality differences in test accuracy might vary as a function of MoCA cut-off score needs further exploration. However, it seems likely that with lower cut-off scores the proportion of undetected cognitive impairment especially for the right hemisphere group would be even higher. Likewise, domain-specific impairment on neuropsychological assessment was defined, following commonly accepted practice, as performance at or below the 5th percentile (between 1.5 and 2 SD). Different cut-offs and operational definitions of impaired performance have been shown to alter sensitivity and specificity of screening measures (13). Future work should examine whether these laterality differences remain when less or more stringent criteria is applied.

As our study used a retrospective sample of clinically collected data, one of the main limitations is that we were not able to evaluate the patients who were excluded from the study to assess for possible biases in our sampling. The clinical relevance of this needs to be further investigated. Related to this, our sample was most likely restricted towards more cognitively-able patients as only those who were able to participate in neuropsychological assessment was included, possibly limiting the generalizability of our results. However, this is unlikely to have impacted on our conclusions as we were particularly interested in examining the cohort of patients who were scoring in the MoCA-intact range. More generally, it is neuropsychological assessment only represents one aspect of assessing cognitive impairment and is constrained by aphasia, as alluded to earlier, but also other factors such as fatigue and visual neglect. It may be helpful in future research to include functional-based cognitive assessments in the analysis of MoCA performance.

5. Conclusion

Overall, our findings show that the MoCA has poor test accuracy for detecting cognitive impairment following right hemisphere stroke but better accuracy for detecting gross left hemisphere stroke cognitive deficits. Particular care needs to be taken in interpreting MoCA performance for right hemisphere stroke patients as they are likely to have impairment that is undetected. Specifically, common impairments in general intellectual functioning, processing speed and visual memory need to be considered separately given they are not assessed by the MoCA. In addition, the MoCA is poor at capturing all impairments in executive/attention functions for both left and right hemisphere stroke patients, possibly due to the complex nature of these cognitive domains. Further work is needed to improve the MoCA's sensitivity for use within the stroke population. The recent development of stroke–specific cognitive screens show promise (22). Alternatively, clinicians could consider supplementing the MoCA with additional screening items or brief assessment tools to overcome some of the limitations identified. Bearing in mind test burden, time limitations and opportunity costs, cognitive assessment post-stroke does not necessarily need to be exhaustive but should be comprehensive in order to maximise the detection of possible impairments.

Conflicts of interest: The authors declare no conflicts of interest.

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