ACCURACY OF THE MONTREAL COGNITIVE ASSESSMENT IN DETECTING COGNITIVE IMPAIRMENT FOLLOWING STROKE

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Abstract

Vascular cognitive impairment (VCI) post stroke is frequent, but may go undetected, which highlights the need to better screen cognitive functioning post stroke. We sought to examine the diagnostic accuracy of the Montreal Cognitive Assessment (MoCA), a cognitive screening measure recommended for use with stroke populations. We assessed cognitive status in 161 individuals who were at least 3 months post stroke with a comprehensive battery of neuropsychological measures. We compared diagnostic accuracy using a single cut point compared to two cut points and determined that sensitivity and specificity were optimal when two cut points were applied. This resulted in three groups, where 27% of participants scored ≤ 23 and were classified as high likelihood of cognitive impairment, and 25% of participants scored ≥ 28 and were classified as low likelihood of cognitive impairment. The remaining 47% of participants scored from 24 to 27 and were classified as indeterminate likelihood of cognitive impairment. The addition of a processing speed measure improved classification for this group by correctly classifying 71% of the individuals in this category. We provide a three-category diagnostic approach to better identify individuals as certain and uncertain likelihood of cognitive impairment. The addition of a processing speed measure provides a practical and efficient method to increase confidence in the determined outcome, while also expanding the utility of the MoCA

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Accuracy of the Montreal Cognitive Assessment (MoCA) in Detecting Cognitive Impairment following Stroke

Cognitive impairment post stroke can result in significant physical and psychological consequences for the individual. These effects, in turn, place a significant financial burden on the health care system (Rockwood et al., 2000). In Canada, stroke is the number one cause of disability in adults, as 30% of men and 40% of women with cognitive impairment post stroke become dependent on institutions for full-time care (Rockwood et al., 2000; Rockwood, Ebly, & Hachinski, 1997). Furthermore, as many as 77% of individuals with stroke with cognitive impairment have been reported to go undetected by cognitive screening measures (Chan et al., 2014). In a 5-year follow-up of individuals with vascular cognitive impairment (VCI), Wentzel and colleagues (2001) found that 46% of individuals without dementia at baseline developed dementia over the study period. This is a similar rate of progression to dementia for individuals with mild cognitive impairment (MCI). These findings highlight the importance of accurate detection of individuals who are at high risk of progressing to dementia due to vascular disease. Early detection can allow for early intervention, which may lead to better functional long-term outcomes for those who are at risk.

Despite its enormous social and economic impact, cognitive impairment post stroke is still not well understood, with no standardized clinical screening criteria for detecting early impairment and identifying at-risk individuals. Furthermore, not all individuals with stroke develop cognitive impairment, and many experience only transient or mild symptoms (Gorelick et al., 2011; Wentzel et al., 2001). Thus, cognitive decline post stroke is not inevitable; variance in cognitive changes may be due to risk factors associated with the onset of stroke and their cerebrovascular mechanisms, as well as the severity and location of the cerebrovascular damage.

Screening Cognition Post Stroke

Best-practice guidelines recommend the use of cognitive screening tests with individuals with stroke (Eskes et al., 2015). Cognitive screening tests are readily available and used with stroke populations in a variety of settings, including primary health care and post-operative settings. These screening measures are typically employed to differentiate cognitive changes that are considered normal from those that represent impairment (Blackburn, Bafadhel, Randall & Harkness, 2012). The Montreal Cognitive Assessment (MoCA) was developed by Nasreddine and colleagues (2005) to help point-of-care physicians detect subtle cognitive changes early in the course of neurodegenerative disease, namely MCI. It is important to note that the MoCA was originally designed to be sensitive to memory changes that differentiate MCI from normal aging (Nasserdine et al., 2005), and memory impairment may not necessarily be characteristic of stroke populations. Nonetheless, it is now a widely used cognitive screening measure, and the test has been recommended by the National Institute of Neurological Disorders and Stroke-Canadian Stroke Network (NINDS-CSN) for use with stroke populations (Hachinski et al., 2006). The convenience of rapid test administration and support across several disease populations including cardiovascular conditions (Hawkins et al., 2014; McLennan, Mathias, Brennan, & Stewart, 2011), Parkinson's disease (Zadikoff et al., 2008; Dalrymple-Alford et al., 2010) and traumatic brain injury (Wong et al., 2013) has increased the use of the MoCA for a variety of clinical populations.

The MoCA can be administered in under 10 minutes and yields a single total score out of 30. According to the authors, scores below 26 reflect possible cognitive impairment. Although the test is designed to yield a global measure of cognitive impairment, the items are generally grouped together based on cognitive domains, and individual subscale scores can be calculated

for each cognitive domain. The test examines eight domains: visuospatial skills, executive functions, object perception, memory, attention, language, abstraction and orientation. The inclusion of items that place demand on executive functions has been viewed as a strength of the MoCA over other screening measures, arguably making it more sensitive to the type of cognitive impairment that is most characteristic of individuals with vascular disease (Cees De Groot et al., 2000; Garrett et al., 2004; Koski, 2013; Price, Jefferson, Merino, Heilman, & Libon, 2005). Although post stroke cognitive impairment profiles can be quite variable depending on stroke location and severity, several studies have found that individuals with cerebrovascular conditions are more likely to lose points on items of executive functions, fluency and recall subtests than on any other subtests of the MoCA (Cumming, Bernhardt, & Linden, 2011; Martinić-Popović, Lovrenčić-Huzjan, & Demarin, 2009; Toglia, Fitzgerald, O'Dell, Mastrogiovanni & Lin, 2011). Similarly, Pendlebury et al. (2012) found that nondemented individuals with stroke performed worse than those without stroke on MoCA items of executive functions, fluency, and attention. These differences on item performance are seen even among those individuals who score within normal limits on other screening measures, such as the Mini-Mental Status Examination (MMSE).

These findings suggest that the MoCA may better detect impairment that is specific to vascular conditions compared to other screening measures. Specifically, the MoCA has been shown to have better sensitivity than the MMSE in a variety of disease populations, including VCI and MCI (Dong et al., 2010; Godefroy et al., 2011;Hachinski et al., 2006; Nasredine et al., 2005; Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010). The MoCA is thought to be more cognitively demanding than the MMSE and therefore less likely to yield ceiling effects and more likely to capture subtle cognitive changes (Godefroy et al., 2011;Hachinski et al., 2006;

Nasredine et al., 2005; Pendlebury, et al., 2010).

Processing Speed

Despite the clear support for the use of the MoCA for cerebrovascular conditions, it does not include a measure of processing speed, which is often affected in stroke populations (Garrett et al., 2004; Patel, Coshall, Rudd & Wolfe, 2003; Rockwood et al., 2000). Speed of information processing can easily be assessed by tests that can be administered in under two minutes. For example, the Symbol-Digit Modalities Test (SDMT; Smith, 1982) was first designed as a screening measure to identify individuals with neurological impairment. It assesses functions such as visual scanning, psychomotor speed, attention and learning. A comprehensive review of the SDMT (Strauss, Sherman, & Spreen, 2006) indicates that the SDMT is one of the most sensitive tests to brain insult in neuropsychology with a large number of studies documenting its utility to detect cognitive impairment, changes in functioning, and disease progression in a variety of disease including the standardized evaluation of traumatic brain injury (Ponsford & Kinsella, 1992), multiple sclerosis (Beatty et al., 1995; Solari et al., 2002), Huntington's disease (Huntington, 1996) and concussion (Erlanger, et al., 2003). In particular, one study found that processing speed, as measured by the SDMT, was one of the domains that best discriminated between cognitively impaired and intact individuals among those with vascular symptoms (Sachdev et al., 2004). The importance of processing speed has also been noted in the MoCA literature. For example, Chan et al. (2014) found that more than 50% of acute stroke individuals were impaired on measures of processing speed, despite scoring in the normal range on the MoCA. Similarly, Pendlebury et al., (2012) attributed the MoCA's low sensitivity in detecting nonamnestic single-domain cognitive impairment to a lack of measuring slowed processing speed.

MoCA Cut Point Accuracy

Several studies have investigated the diagnostic accuracy of the MoCA using the traditional cut point of 26, with scores ≥ 26 considered in the normal range and scores ≤ 25 indicative of cognitive impairment. However, this dichotomous approach may lead to a reliance on using the screening test as a diagnostic tool in diagnosing cognitive impairment (Webb et al., 2014) instead of as a screening measure. In some research studies, the MoCA has been used to reflect severity of cognitive impairment rather than likelihood by specifying a set range of scores to reflect mild or severe cognitive impairment (Webb et al., 2014). Using a single cut point to determine dichotomous outcomes may not accurately capture the range of functioning in a clinical setting. False negatives, in particular (i.e., identifying cognitively impaired individuals as intact), may result in a failure to follow up with further investigations and a failure to treat or intervene where necessary (Wong et al., 2015). An alternative method of screening, using receiver operator characteristics (ROC) curves, is to create multiple-group classifications to compare functioning across a range of diagnostic certainty (Attwood, Tian, & Xiong, 2014; Nakas, Alonzo, & Yiannoutsos, 2010). Indeed, Swartz and colleagues (2016) suggested a three-group classification approach using ROC curves to determine optimal sensitivity and specificity cut points for the MoCA for individuals with cerebrovascular symptoms to create a more useful classification screening system. This approach identifies individuals as low likelihood (above the top cut point), high likelihood (below the bottom cut point), and indeterminate likelihood (between the two cut points) of cognitive impairment. This three-group approach is useful for categorizing individuals who have a high probability of being intact or impaired, but it also leaves a group of individuals between the two cut points as unknown or indeterminate likelihood of having cognitive impairment. In the latter case, a more detailed assessment would be needed

to determine the presence or absence of cognitive impairment.

In the present study, we sought to confirm the three-group classification approach using ROC curve analysis to identify post-acute stroke individuals that are at low, high or indeterminate likelihood of cognitive impairment as identified by a gold-standard, detailed neuropsychological assessment. To improve classification and reduce the number of people in the indeterminate category, we conducted two additional analyses. First, we examined whether performance on specific subdomains of the MoCA provides more information than using the single global score to categorize individuals in the indeterminate category. Second, we examined the inclusion of processing speed using the SDMT, in addition to the MoCA total score, to examine whether this provides additional predictive utility to the MoCA.

Method

Participants

Participants were obtained from the Ontario Neurodegenerative Disease Research Initiative (ONDRI), which is an ongoing longitudinal, multidisciplinary research study investigating common profiles among five neurodegenerative conditions (Farhan et al., 2017). Only the vascular cognitive impairment (VCI) cohort was used in the present study. All participants were tested across various assessment platforms including genomics, neuroimaging, ocular function, and gait and balance, as well as language and neuropsychological testing. Demographic, clinical, and neuropsychological data obtained from the first, baseline assessment were used for this study. All participants were administered the MoCA as part of the screening procedure, and the neuropsychological battery was administered within 8 weeks of initial screening with the MoCA.

All participants provided informed consent and met extensive eligibility criteria for the

larger ONDRI study (Farhan et al., 2017). All participants in the VCI cohort also met the following inclusion criteria: (a) proficient in speaking and understanding English, with self-ratings of 7 or more (corresponding to "good") for both speaking and understanding English on the Language Experience and Proficiency Questionnaire (Marian, Blumenfeld, & Kaushanskaya, 2007), (b) eight or more years of formal education, (c) post-acute (≥ 3 months) ischemic stroke or silent stroke that was documented on MRI or CT, (d) mild-moderate stroke severity defined by scores of 0-3 on the modified Rankin Scale (Bonita & Beaglehole, 1988; Rankin, 1957), and (e) a MoCA score of at least 18. Exclusion criteria included a history of dementia prior to the stroke, large cortical strokes, severe cognitive impairment, aphasia, inability to write, or severe functional disability limiting ability to perform the assessment.

Participant Characteristics

Participant characteristics are provided in Table 1. There was a total of 161 participants with approximately a 1:2 ratio of women to men. Participants were in their late 60s on average and had some university education (M = 14.5 years).

Assessments

The MoCA is a 49-item cognitive screening test with a possible score range of 0 to 30. It assesses eight cognitive domains, as listed in Table 2 and included in the appendix. As per the published scoring protocol (Nasreddine et al., 2005), an education correction of one additional point is applied to the total score for participants with ≤ 12 years of education.

The SDMT is a 110-item substitution task that is used to assess processing speed and incidental learning. The test consists of symbols that are matched to numbers from 1 to 9 according to a key printed at the top of the test form. First the participants were presented with a series of symbols, and asked to write the numbers with which the symbols are associated as

quickly as possible in 90 seconds. The score is the total number of items filled in correctly during the time limit (max = 110). The second part of the test consisted of a line of 15 symbols in which all 9 original symbols were included at least once. Participants were asked to fill in the number associated with that symbol, from memory, without the assistance of the key. The score is the number of items recalled correctly during the time limit (max = 15). In cases where a symbol was presented more than once, and the participant correctly identified the number on one occasion and incorrectly identified it on another, the participant was given credit for the correct identification. The purpose of this was to assess the incidental learning component of the task. Therefore, two scores were obtained for the SDMT: speeded processing and recall (learning).

The neuropsychological assessment consisted of a standardized battery administered to all participants. The tests were categorized into six cognitive domains based on a principle component analysis (Troyer et al., 2017), as shown in Table 3. Test scores were normalized based on age, education, and sex using published norms from their respective test manuals and converted to standardized scores. Participants were deemed cognitively impaired on the neuropsychological battery if they obtained a standardized score that was lower than 1.5 standard deviation (SD) below the mean on at least two tests within one or more domains.

Statistical Analyses

All statistical analyses were conducted in SPSS Version 22.0. Descriptive characteristics were examined to calculate the effects of age, education and sex on MoCA scores. To examine performance on the neuropsychological battery, we identified participants scoring in the normal range on the MoCA using the traditional cut point of MoCA ≥ 26 and investigated their performance on the neuropsychological tests and cognitive domains. Our primary analysis consisted of calculating measures of diagnostic accuracy of the traditional cut point score of ≥

26, including sensitivity, specificity, positive and negative likelihood ratios, and positive and negative predictive values. We then used ROC curves to maximize sensitivity and specificity to determine an optimal single cut point, and to determine a three-group classification with two cut points: one with high sensitivity and a second with high specificity. Participants scoring below the high sensitivity cut point were classified as high likelihood for cognitive impairment, and participants scoring above the high specificity cut point were classified as low likelihood. Participants scoring between the two cut points were classified as indeterminate or unknown likelihood of cognitive impairment. Measures of diagnostic accuracy were calculated for all cut point analyses.

To improve classification for the indeterminate group, a second analysis was conducted using discriminant function analysis to build a predictive model for group membership to correctly classify participants as impaired or not impaired as determined by their performance on the neuropsychological battery. We examined two sets of variables to create two separate discriminant functions. First, we examined the predictive value of distinct MoCA subdomain items, rather than the total MoCA score, to investigate if scores on specific cognitive domains of the MoCA better characterize participants in each group. Secondly, we examined the utility of SDMT, paired with the total MoCA score, to examine whether the additional metric of performance on processing speed and incidental learning allows for more accurate discrimination of participants' cognitive status than using their MoCA total score alone. Participants from the high and low likelihood of cognitive impairment groups were used first to develop the discriminant functions, and then the models were tested on the indeterminate group. The cross-validated classification method was used to indicate the final number of cases correctly identified by each function. This method employs the leave-one-out technique in which one case is

systematically held out and the discriminant analysis is performed on the remaining sample. Then, the excluded case is classified into one of the groups based on the discriminant function and the procedure is repeated on each case of the sample until all cases are classified. This results in a more conservative estimate of the number of cases correctly identified by the function (Brown & Wicker, 2000). This method was used to indicate the number of cases correctly identified based on the predictor variables in the model.

Results

Neuropsychological Data

Of the 161 participants, 100 (62%) met the criterion for cognitive impairment (≥ 1.5 SD on ≥ two subtests in at least one domain) on the neuropsychological battery. Fifty-six participants (35%) were impaired on two or more cognitive domains, and 21 (13%) were impaired on three or more domains. As seen in Table 3, among those who were impaired on at least one domain, processing speed and memory were the most frequently impaired domains. The visual spatial domain was the third most common impairment, whereas fewer than 10% of the participants were impaired on language, attention and object perception.

The Brief Visuospatial Memory Test (BVMT) loaded on to two cognitive domains, namely memory and visual-spatial, in the original PCA (Troyer et al., 2018). Ten individuals were impaired on only the BVMT variables. In order to determine whether that impaired performance should be classified in the memory or visual-spatial domain, these ten cases were individually reviewed by two clinical neuropsychologists. Although no additional test variables met the criterion of 1.5 SD below the mean or lower, we considered performance around 1 SD below the mean to indicate a relative weakness in that domain. Seven of the 10 participants showed this level of performance on at least one additional memory or visual-spatial variable.

The remaining 3 participants performed well within the normal range on all other variables. Because the BVMT variables load slightly more highly on the memory domain than the visual-spatial domain in our earlier work (Troyer et al., 2017), their impaired level of BVMT performance was interpreted as reflecting memory impairment.

MoCA Performance

The mean MoCA score was 25.3, with 47% of participants scoring below the traditional cut point of 26 and 53% participants scoring at or above the cut point. In a multivariate regression model, age and education were significant predictors of MoCA score (R^2 = .095, p < .001), where older participants (β = -0.102, p < .001) and those with fewer years of education (β =.186, p = .022) had lower MoCA scores. Sex (β = .028, p = .955) did not significantly predict MoCA scores. Table 4 presents a frequency count of the number of participants who were cognitively impaired or intact based on the neuropsychological battery as a function of MoCA score.

Next, we examined neuropsychological performance of the MoCA pass (≥26) and MoCA fail (≤25) groups based on the recommended cut point of 26. Of the 86 individuals in the MoCA pass group, 36 (42%) were impaired on at least one of the neuropsychological domains. Regarding the areas of impairment, 26 (30%) participants were impaired on speed, 17 (20%) were impaired on memory, 6 (7%) were impaired on visual perception, 1 (1%) was impaired on language, 1 (1%) was impaired on attention, and 8 (9%) were impaired on object perception. Of these 86, 15 (17%) were impaired on two or more domains, and 7 (8%) were impaired on three or more domains on the neuropsychological battery.

Of the 75 individuals in the MoCA fail group, 64 (85%) were impaired on at least one of the neuropsychological domains. Thirty-nine (52%) were impaired on speed, 47 (63%) were

impaired on memory, 13 (17%) were impaired on visual perception, 13 (17%) were impaired on language, 5 (7%) were impaired on object perception and no individual was impaired on the attention domain. Of these individuals, 41 (55%) were impaired on two or more domains, and 14 (19%) were impaired on three or more domains.

Measures of Diagnostic Accuracy Analysis

Using the traditional single cut point of MoCA ≥ 26, sensitivity was 64% and specificity was 82%. Our ROC analysis indicated that the optimal single cut point, which maximized sensitivity and specificity, was for MoCA ≥ 27. The optimal two cut points were MoCA ≤ 27 (to maximize sensitivity) and MoCA ≥ 24 (to maximize specificity). All results are summarized in Table 5. Using two cut points, 27% of participants scored ≤ 23 and were classified as high likelihood for cognitive impairment, and 25% of participants scored ≥ 28 and were classified as low likelihood for cognitive impairment. The remaining 47% of participants scored in the range of 24 – 27 and were classified as indeterminate likelihood for cognitive impairment.

Discriminant Function Analysis

Discriminant function analysis (DFA) was used to examine the usefulness of MoCA subdomain scores in predicting whether individual domains of the MoCA were better at discriminating individuals in the indeterminate MoCA group as impaired or not impaired on the neuropsychological battery. Eight MoCA variables were created by grouping scorable items into their respective cognitive domains determined by consensus of two neuropsychologists, as shown in Table 2. The discriminant function was significant, $\Lambda = .49$, $\chi^2(8) = 55.26$, $p < .001$, accounting for 51% of between-group variability. Analysis of the structure matrix correlation coefficients which reveal the strength of each variable with the function indicated that items of delayed recall ($r = .725$), attention ($r = .562$), visual reconstruction ($r = .447$), language fluency

(r = .411), immediate memory recall (r = .354), and abstraction (r = .341) were significant group predictors, whereas object naming and orientation did not reach significance, r < .30 (Brown & Wicker, 2000). The cross-validated classification showed that overall, 67 of 84 cases in the high or low groups, or 80%, were correctly identified based on the predictors in the model, as shown in Table 6. Next, in order to test the predictive utility of the model, we conducted a discriminant function analysis on the indeterminate MoCA group alone. The discriminant function for the indeterminate group was not significant, Λ = .820, χ^2 (8) = 13.49, p = .096, and accounted for 18% of between-group variability.

Next, we examined the predictability of the MoCA total score paired with the SDMT. The SDMT was removed from the neuropsychological battery before conducting analyses. This changed cognitive status for two participants who were originally impaired on the SDMT and only one other measure in the speed domain on the neuropsychological battery. Once the SDMT was removed, these two participants no longer met criteria for cognitive impairment on the neuropsychological battery.

We entered two subscores from the SDMT in the DFA, a speed subscore and a learning subscore. The discriminant function was significant, Λ = .512, χ^2 (3) = 54.55, p < .001, accounting for 49% of between-group variability when tested on the high and low likelihood of cognitive impairment groups. Analysis of the structure matrix scores revealed that the MoCA total score and SDMT speed score were significant group predictors, rs = .979 and .685, respectively, whereas the SDMT learning score did not reach significance, r = -.096. The cross-validated classification showed that overall, 70 of 85 cases, or 82%, were correctly identified, as shown in Table 7. Next, we tested this model for the indeterminate group alone. The discriminant function for the indeterminate group was also significant, Λ = .842, χ^2 (3) = 12.48, p < .01,

accounting for 16% of between-group variability. Analysis of the structure matrix revealed that the MoCA total score, SDMT speed score, and the SDMT learning score were all significant predictors of group membership for the indeterminate group, *r*s = .833, .593, and .543, respectively. The cross-validated classification showed that overall, 54 of 76 cases, or 71%, were correctly identified for this group, as shown in Table 8.

Discussion

Recommendations for screening cognitive impairment post stroke pose a challenge as the standard evaluation must accommodate disease heterogeneity but also be specific and feasible in a clinical setting. Although there is no single neuropsychological impairment profile for cognitive impairment post stroke, executive dysfunction and slowed processing speed are two prominent features of both VCI and vascular dementia. Therefore, these two domains should be assessed when screening for cognitive impairment post stroke. The MoCA was developed to detect mild cognitive impairment in neurodegenerative disease, with the original study based on a cohort of participants recruited from memory clinics (Nasreddine et al., 2005). It is a more sensitive test than the MMSE in detecting MCI, and it holds promise for detecting VCI because, unlike the MMSE, it includes items assessing executive functions.

The strategy for cognitive screening should be informed by the purpose of the clinical or research question. If the purpose of the initial screening is to pick-up all potential cases to allow for further assessment, then using a measure that is highly sensitive (low rate of false negatives) may be preferable. This ensures that those at high likelihood of impairment will receive appropriate treatment. It could be argued that for initial screening, sensitivity is often preferred compared with specificity. However, in a clinical setting false positives may pose a costly outcome when busy clinics and expensive treatments are used for individuals who do not need

them. As such our findings in this study directly address these issues by helping to correctly identify those who need the resources and those who do not.

We propose that using a three-group approach to identifying individuals at risk of cognitive impairment closely represents the thought process in a clinical setting. Identifying individuals who are at low, intermediate, and high likelihood of cognitive impairment is an effective method of triaging, where clinicians can be highly certain in their decision to determine which individuals should be sent for neuropsychological referrals. We found that using two cut points rather than a single cut point for the MoCA allowed us to increase the test's sensitivity and specificity to higher than 90%. Individuals who scored > 27 and < 24 made up our low and high likelihood of cognitive impairment groups, respectively. This means that the cognitive status determined by performance on the neuropsychological battery was correctly identified by the MoCA for more than 90% of individuals within these two groups. While this approach improves the diagnostic accuracy of the MoCA compared to the single cut point approach, where both sensitivity and specificity were below 80%, almost half of our participants scored in the middle range of the MoCA, between the two cut points. Thus, we were uncertain of the likelihood of cognitive impairment for almost half of the participants in our sample, based on their MoCA score alone. In studies favoring the single cut point, there is great variability in the range of reported cut points varying from scores ≤ 19 to ≤ 26 (Cumming et al., 2011; Dong et al., 2010; Dong et al., 2012; Godefroy et al., 2011; Lees et al., 2014; Pendlebury et al., 2010; Salvadori et al., 2013; Wong et al., 2009; Wu, Wang, Ren, & Xu, 2013). This variability can in part be explained by choosing to favor either optimal sensitivity or specificity, or choosing an arbitrary "optimal" point to balance both sensitivity and specificity, compromising the overall accuracy of the test. Additionally, it is important to acknowledge that cognition is inherently a

complex phenomenon which is difficult to measure with screening measures, and therefore variability in performance should be expected. Several noncognitive factors such as mood, fatigue, age, education, and motivation have been reported to contribute to fluctuating scores on various tests of cognition (Visser-Keizer, Jong, Deelman, Berg, & Gerritsen, 2002). With the three-group approach we directly address this heterogeneity and better divide individuals into certain and uncertain likelihood of cognitive impairment to help clinicians determine appropriate candidates for further testing.

Using this approach, three groups emerged: those who are at high likelihood of cognitive impairment, those at low likelihood of cognitive impairment, and those with indeterminate likelihood. With this approach, only individuals who fall in the indeterminate group require further assessment. The high likelihood group was the most homogenous group, where most of the participants were impaired on the neuropsychological battery and correctly identified by the MoCA. The low risk group had more variability with some participants who had MoCA scores of ≥ 28 but were identified as impaired on the neuropsychological battery. Lastly, the intermediate group emerged as the largest group and consisted of approximately half of our sample, where almost two-thirds of them had impairment on the neuropsychological battery.

To address the unknown likelihood of cognitive impairment of the indeterminate group, we found that pairing an additional neuropsychological test, the SDMT, with the total MoCA score improved classification for this group, such that the majority of cases in this uncertain range were correctly identified. We found that both the processing speed and learning subscores of the SDMT provided discriminant utility for the indeterminate group, whereas only the processing speed subscore was useful in categorizing individuals in the certain (high and low likelihood) groups. The added discriminant utility of processing speed with the MoCA is

consistent with past research that suggests slowed processing speed is characteristic of cognitive impairment post stroke. Our findings suggest that where resources are limited and to avoid unnecessary referrals, employing an additional quick 90-second processing speed measure can increase confidence in the determined outcome. This approach is both practical and efficient, as many processing speed measures are readily available (such as the SDMT used by us) and can be completed in under 2 minutes in any clinical setting, making them an ideal addition to a screening test. While the incidental learning subscore was also significant in discriminating cognitive impairment, it was only significant for the indeterminate group. Although some studies have reported impaired visual and verbal learning in vascular dementia (Sachdev et al., 2004), incidental learning is not commonly assessed. Studies that have used the SDMT with VCI, and report impairment on the test, do not clarify if both trials, the incidental learning and processing speed were administered (Pendlebury et al., 2012; Sachdev et al., 2004). This warrants further investigation to determine whether subtle changes in incidental learning may be a domain of early cognitive impairment in post stroke individuals. Nonetheless, the discriminant utility of processing speed suggests that this domain should be assessed post stroke.

Adding processing speed also expands the domains assessed by the MoCA to detect impairments in populations other than the one it was originally designed for (i.e., MCI). This crucial cognitive domain is often impacted in several disorders (e.g., multiple sclerosis, Parkinson's disease, Huntington's disease; Zadikoff et al., 2008; Dalrymple-Alford et al., 2010), and has been reported as a critique of the MoCA's reduced sensitivity for those with vascular disease (Chan et al., 2014; Pendlebury et al., 2012) The addition of the SDMT directly addresses these concerns, while also appropriately extending the use of the MoCA so it is efficient in detecting impairment that is characteristic of the population that it is being used for.

We also found that examining individual subdomains of the MoCA did not significantly improve its ability to discriminate cognitive impairment for the indeterminate group. This further reflects the heterogeneity of vascular disease, and as such no distinct pattern of individual subdomains of the MoCA was better at identifying individuals in the indeterminate category. This also further speaks to the heterogeneity inherent in screening cognition. Although there is a group of individuals who can be classified with certainty by using maximum sensitivity and specificity cut points, there remains a sub-group whose cognitive abilities remain undetermined by quick screens, even with the addition of a processing speed measure that improves classification of the indeterminate group by more than two-thirds. No screening tool can be perfect, so there will always be a subgroup that warrants further assessment. Given the cost in terms of time, money, and medical resources of conducting a comprehensive neuropsychological battery, the goal is to reduce this subgroup as much as possible.

This study represents a pragmatic approach, with a clean sample of post-acute stroke individuals and a large sample size; nevertheless, there are some limitations to our design. First, the study required volunteers and thus this self-selection process may have resulted in participants that are not best representative of the general post-acute stroke population. Participants may have been higher functioning than seen in the general clinic by virtue of the study requirements: they had to have sufficient motor, language, hearing and visual functioning to complete neuropsychological testing. Additionally, we used a definition of cognitive impairment that best represents mild-moderate risk of ≥ 1.5 SD on two or more tests in a single domain (often used in mild cognitive impairment literature) rather than severe impairment, thus resulting in a higher prevalence rate of cognitive impairment in our sample than other studies that used a more conservative definition (i.e. ≥ 2 SD). However, only a little over half of our

sample was cognitively impaired using our definition, suggesting that we had good variability of cognitive performance in our sample where our impaired and intact groups were close to equal. This is important because the prevalence rate of disease (i.e., cognitive impairment in our case) directly affects the predictive value of a test. Additionally, our criteria requiring impairment on two or more tests within a single domain, rather than one test, was designed to identify individuals with single domain cognitive impairment that are unlikely to be found by chance alone, and who would more likely require clinical assessment to determine their prognosis of cognitive functioning. Finally, the cognitive domains used in our definition of cognitive impairment were based on a principle component analysis determined on this sample. This restricts the generalizability of the results to other diseases, as the same tests might not load together to form the same cognitive domains in different disease cohorts.

Future research should examine the utility of the SDMT as a stand-alone screening measure for post stroke individuals. As mentioned earlier, the test was originally designed as a screening tool (Smith, 1982), and it is highly sensitive to brain insult. Although we were interested in using the test for its measure of processing speed, the processing speed trial could also be assessing attention, visual scanning, and memory, thus, these functions may contribute to task performance. It could also be possible that these domains, as well as incidental learning may be sufficient in discriminating early cognitive impairment in vascular disease, as suggested by the significance of incidental learning in our results. In addition, it would be useful to investigate the discriminate utility of a range of processing speed measures to better tease apart the role of processing speed and other cognitive domains affected in vascular disease.

In conclusion, we provide a clinically useful approach to stratify post-acute stroke individuals into three groups forming homogenous groups of low and high likelihood of

cognitive impairment as well as a group in the intermediate range. These groups form useful clinical categories to separate those who may need to be prioritized with immediate attention in the high likelihood group, from those who should be sent for further assessment in the indeterminate group, while also identifying those who do not require immediate management and are unlikely to have cognitive impairment in the low likelihood group. We further provide a practical and efficient method to increase certainty of cognitive impairment for the indeterminate group while also expanding the domains assessed by the MoCA by pairing it with an additional processing speed measure. Our results show that with the inclusion of the SDMT with the MoCA total score we could correctly discriminate cognitive status for majority of the individuals in the indeterminate category. This approach helps to expand the MoCA for use with stroke populations, while also improving the breadth of the test without compromising the qualities of a screening tool. This provides an efficient method to increase the diagnostic accuracy of the MoCA allowing clinicians to better detect individuals in need of further assessment.

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Table 1

Participant Characteristics

All Participants (n = 161)		
	M (SD)	*n*
Age, years	68.7 (7.4)	
Education, years	14.5 (2.9)	
Sex		
Male		110 (68%)
Female		51 (32%)
MoCA score	25.3 (3.1)	
MoCA impairment (< 26)		75 (47%)
MoCA indeterminate group (scores 24 – 27)		76 (47%)
NP impairment		100 (62%)

Note. NP impairment = ≥ 1.5 SD below the mean on ≥ 2 subtests within a cognitive domain

Table 2

MoCA Domain Items

MoCA Domains	Individual MoCA Items and Points Per Item	Total points Per Domain
Attention	Forward digit span (1)	10
	Backward digit span (1)	
	Tap for each letter A (1)	
	Serial 7 subtraction (3)	
	Repeat first sentence (1)	
	Repeat second sentence (1)	
Delayed recall	Recall with no cue (5)	15
	Recall with category cue (5)	
	Recall with multiple choice cue (5)	
Visual construction	Trails (1)	5
	Cube copy (1)	
	Clock drawing (3)	
Abstraction	Similarity (2)	2
Language Fluency	Raw number of words generated for fluency (25)	25
Immediate recall	First trial of recall (5)	10
	Second trial of recall (5)	
Object Naming	Naming 3 animals (3)	3
Orientation	Date (1)	6
	Month (1)	

Year (1)

Day (1)

Place (1)

City (1)

Table 3

Neuropsychological Data

Neuropsychological Domain	Tests included	Number (and percent) of participants impaired[a]
Speed	Symbol-Digit Modalities	65 (40%)
	Trail Making Test, Part A	
	Trail Making Test, Part B	
	Stroop Colour Naming	
	Stroop Word Reading	
	Stroop Inhibition	
	Stroop Switching	
	Verbal Fluency Letters	
	Verbal Fluency Categories	
Memory	Rey Auditory Verbal Learning Test Immediate recall	64 (40%)
	Rey Auditory Verbal Learning Test delayed recall	
	Rey Auditory Verbal Learning Test recognition hits	
	Brief Visuospatial Memory Test immediate recall	
	Brief Visuospatial Memory Test delayed recall	
	Brief Visuospatial Memory Test recognition discrimination	
Visual Spatial	Wechsler Adult Intelligence Scale Matrix Reasoning,	19 (12%)
	Judgment of Line Orientation	

	Brief Visuospatial Memory Test immediate recall	
	Brief Visuospatial Memory Test delayed recall	
Language	Wechsler Adult Intelligence Scale Vocabulary	14 (9%)
	Boston Naming Test	
	Verb Naming	
	Semantic Probe	
Attention	Digit-Span Backwards	1 (1%)
	Digit-Span Forward	
	Digit-Span total	
Object Perception[b]	Incomplete Letters	13 (8%)

[a] Impairment = ≥ 1.5 SD below the mean on ≥ 2 subtests within a cognitive domain.
[b] This domain was considered impaired if individuals were impaired on the single test within the domain (incomplete letters)

Table 4

Number of Participants Impaired vs. Not Impaired on the Neuropsychology Battery as a Function of MoCA Score

MoCA Score	Impaired (*n*)	Not impaired (*n*)
18	2	0
19	8	0
20	7	0
21	3	1
22	7	0
23	12	4
24	13	2
25	12	4
26	15	7
27	12	11
28	5	10
29	3	14
30	1	8
Total	100	61

Table 5

Diagnostic Accuracy Analysis and Optimal Cut Points

Diagnostic Characteristics	Traditional Cut Point ≥ 26	Single Optimal Cut Point ≥ 27	Two Optimal Cut Points Sensitivity: ≤ 27 Specificity: ≥ 24
Sensitivity	64%	79%	91%
Specificity	82%	70%	91%
PPV	85%	81%	89%
NPV	58%	67%	78%
+LR	3.55	2.68	4.76
-LR	0.44	0.30	0.17
Participants below cut point	75 (47%)	97 (60%)	<24 = 44 (27%) >27 = 41 (25%)

Table 6

Predicted Group Membership Based on MoCA Domains for High and Low Groups

		Classification by DF		
	NP impaired	No	Yes	
Count	No	32	5	37
	Yes	12	35	47
%	No	86.5	13.5	100.0
	Yes	25.5	74.5	100.0

Note. 80% of cross-validated grouped cases correctly classified; NP impaired = cognitive status based on neuropsychological battery

Table 7

Predicted Group Membership using MoCA Total Score and SDMT for High and Low Groups

Cross-Validated Classification Results High and Low Groups				
		Classification by DF		
	NP impaired	No	Yes	
Count	No	32	5	37
	Yes	10	38	48
%	No	86.5	13.5	100.0
	Yes	20.8	79.2	100.0

Note. 82% of cross-validated grouped cases correctly classified; NP impaired = cognitive status based on neuropsychological battery

Table 8

Predicted Group Membership using MoCA Total Score and SDMT for Indeterminate Group

Cross Validated Classification Results Indeterminate Group				
		Classification by DF		
	NP impaired	No	Yes	
Count	No	11	15	26
	Yes	7	43	50
%	No	42.3	57.7	100.0
	Yes	14.0	86.0	100.0

Note. 71% of cross-validated grouped cases correctly classified; NP impaired = cognitive status based on neuropsychological battery

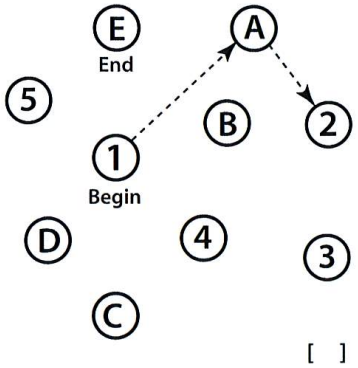
Appendix

Participant Visit ID: _____

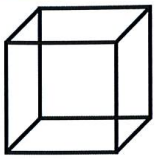
Date: _____

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

VISUOSPATIAL / EXECUTIVE — POINTS



Copy cube



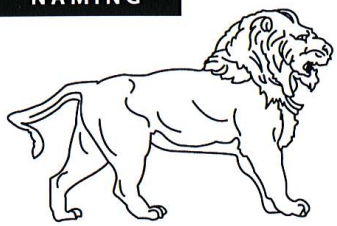
[ ] [ ]

Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

__/5

NAMING



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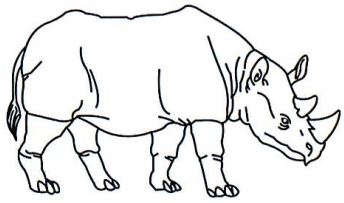

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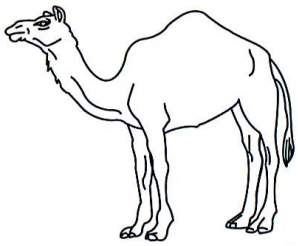

[ ]

__/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

__/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

© Z.Nasreddine MD **www.mocatest.org** Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Completed by: Initials & Date: _____