Serial Montreal Cognitive Assessments Demonstrate Reversible Cognitive Impairment in Patients With Acute Transient Ischemic Attack and Minor Stroke

Leka Sivakumar, MSc; Mahesh Kate, MD, DM; Thomas Jeerakathil, MD, MSc; Richard Camicioli, MD; Brian Buck, MD, MSc; Ken Butcher, MD, PhD

Background and Purpose—Cognitive changes after ischemic stroke are often overlooked, particularly acutely and in patients with mild or transient deficits. We assessed patients with transient ischemic attack (TIA)/minor stroke with serial cognitive screening tests. We tested the hypothesis that mild acute deficits are transient and improve after TIA/minor stroke.

Methods—Patients with acute TIA/minor ischemic stroke, without a history of cognitive impairment, presenting with a National Institute of Health Stroke Scale score ≤3 were assessed <72 hours of onset. Patients were administered the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) at days 1, 7, 30, and 90. Cognitive impairment was defined as MoCA <26 and MMSE ≤26.

Results—One hundred patients with a median (interquartile range) National Institute of Health Stroke Scale score of 1 (2) and median age of 68 (20) years were included. Baseline median MoCA score (26 [4]) was lower than the MMSE (29 [2]; P<0.0001). Cognitive impairment was detected in 54 of 100 patients (54%) with MoCA and 16 of 100 (16%; P=0.001) with MMSE. MoCA scores improved at day 7 (27 [5]), day 30 (28 [2]), and day 90 (28 [2]; P<0.0001). Resolution of cognitive deficits was because of resolution of recall deficits.

Conclusions—Acute temporary cognitive impairment after TIA/minor stroke is common. The MoCA is sensitive to these changes, but the MMSE is not. Routine cognitive assessment after TIA/minor stroke may be warranted and relevant to return to activities even when other neurological deficits are not evident. (Stroke. 2014;45:1709-1715.)

Key Words: ischemic attack, transient ■ mild cognitive impairment

Long-term cognitive impairment is a well-known consequence of ischemic stroke. Approximately two thirds of patients develop cognitive impairment within 3 months of stroke. A history of transient ischemic attacks (TIAs) and minor strokes is also associated with vascular cognitive impairment. Cognitive changes are often overlooked or not assessed in the acute setting. Although detailed neuropsychological testing is ideal, it is time-consuming and impractical in the large TIA/minor stroke population.

Screening tests for cognitive impairment include the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). The MMSE, originally designed to screen for dementia of the Alzheimer type, is currently widely used to assess for poststroke cognitive impairment. Previous studies have indicated that MMSE has reduced sensitivity for mild cognitive deficits and those associated with right-hemisphere lesions. In contrast, the MoCA was developed more recently to detect mild cognitive impairment with higher sensitivity. This assessment has demonstrated high test–retest reliability, good internal consistency, and a particular strength in detecting executive function, a subtest not assessed by MMSE. Although previous studies have compared these assessments in acute ischemic stroke, acute changes in specific cognitive domains after TIA/minor stroke have not been characterized.

In this prospective observational study, we tested the hypothesis that the MoCA is more sensitive than MMSE to acute cognitive changes after TIA/minor stroke. Using serial assessments, we also assessed the temporal pattern of overall and domain-specific cognitive changes within 90 days of TIA/minor stroke.

Methods

Patients

Patients with acute TIA/minor ischemic stroke with a National Institute of Health Stroke Scale (NIHSS) score ≤3 at admission and aged ≥18 years were recruited within 72 hours of symptom onset. Patients were recruited from the Emergency Department at the University of Alberta hospital between July 2008 and April 2013. Exclusion criteria included stroke mimics (ie, seizures, migraine) and acute infections or other acute medical conditions that might be associated with delirium, severe aphasia (>1 on NIHSS item 9), or a prior history of dementia. Preexisting dementia was ruled out with a functional assessment at baseline and a corroborative history from ≥1 relative/neighbor. Subjects who were unable to complete baseline neuropsychological testing were excluded. Informed consent was obtained from all patients before enrollment. This
was an observational study, and secondary stroke prevention measures were implemented in accordance with current practice guidelines.13

Clinical Assessment
All patients underwent a clinical evaluation at days 1, 7, 30, and 90. Stroke syndromes were classified using the Oxfordshire Community Stroke Project system.14 Etiological classification was completed using the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, by day 90.15 At each visit, the MMSE and the MoCA were administered by the physician or trained study team member. Identical versions of the MoCA were administered at all time points. Each MMSE version differed with respect to words used in recall and the orientation of shapes to be copied. The order of testing at each visit was fixed with the MMSE administered first, followed by the MoCA. Patients with <12 years of education were assigned 1 additional point on their MoCA score.12 Patients with an MMSE ≤26 or MoCA score <26 were considered cognitively impaired.7

Neurological function was assessed with the NIHSS score at each time point. Functional outcome was assessed with the modified Rankin Scale (mRS) at days 7, 30, and 90. All raters were certified in NIHSS and mRS administration.16,17 Mood was assessed with the Geriatric Depression Scale18 at days 7, 30, and 90.

Statistical Analysis
Data were analyzed using Statistical Package for Social Sciences version 20.0.0 (SPSS Inc, 2007). Changes in MoCA and MMSE scores between days 1 and 90 were tested using Freidman test followed by post hoc analysis with Wilcoxon signed-rank tests. For both the MMSE and the MoCA, performance within each cognitive domain was calculated as a percentage score (median score/maximum possible score) to allow for relative comparisons between domains and assessments. A linear regression model was used to assess the relationship between baseline domain impairments and cognitive function after 30 days. Spearman correlation was calculated to assess the relationship between both NIHSS and mRS scores and cognitive function. A P value of <0.05 was considered significant.

Results
Patient Characteristics
A total of 118 patients with TIA/minor stroke were enrolled in the study and 18 patients were excluded. The most common reason for exclusion was the presence of known preexisting dementia. The remaining 100 patients (68% men) had a median (interquartile range) NIHSS score of 1 (2) on admission and median population age of 63 (20) years. Of these patients, 19% had a prior history of stroke/TIA. The distribution of stroke syndromes (Oxfordshire Community Stroke Project)14 was partial anterior circulation (57%), lacunar (34%), and posterior circulation (9%). Stroke pathogenesis using TOAST criteria were undetermined (37%), large artery atherosclerosis (25%), cardioembolic (21%), small vessel disease (13%), and other determined causes (4%).15

MoCA Versus MMSE
Median (interquartile range) MoCA and MMSE scores at baseline were 26 (4) and 29 (2), respectively (P<0.0001). The MoCA indicated cognitive impairment in 54 of 100 patients (54%) at baseline. At the same time, the MMSE detected impairment in only 16 of 100 (16%; P=0.001). Thus, 38% of patients with cognitive impairment present at baseline went undetected by MMSE (Figure 1).

Temporal Pattern of Cognitive Changes
Median MoCA scores progressively increased after the onset of symptoms. At days 7, 30, and 90, MoCA scores were 27 (5), 28 (3), and 28 (3), respectively. Median MMSE scores at the same time points remained stable at 29 (2). Wilcoxon signed-rank test indicated a significant improvement in MoCA scores between baseline and day 90 (P<0.0001), whereas MMSE scores remained the same after 90 days (P=0.591).

Cognitive Domains
Assessment subtests were used to analyze performance in specific cognitive domains. The MoCA was divided into 7 cognitive domains, which included orientation, attention, recall, naming, visuospatial, language, and abstract reasoning. The MMSE was divided into 6 cognitive subtests assessing orientation, attention,
recall, language, registration, and constructional praxis. Mean (SD) raw scores and percentage scores for each subtest are summarized in Table 1.

Baseline MoCA assessments indicated that the performance of patients with TIA/minor stroke was poorest in language and recall domains (Figure 2). Although language subtest scores remained stable over 90 days, recall and abstract reasoning subtest scores improved by day 7 and remained stable until day 90. When assessed with MMSE, cognitive performance was poorest in the constructional praxis and recall domains at baseline. Recall performance worsened at day 7 and then gradually improved at days 30 and 90 (Figure 2). Deficits in the other 5 cognitive domains were stable between baseline and day 90.

Four cognitive domains were directly comparable between the MoCA and MMSE: attention, language, recall, and orientation. The greatest difference between the 2 assessments at baseline was in recall (27.5%; \( P=0.014 \)) and language (28.3%; \( P<0.0001 \)) domains (Figure 3). At baseline, the performance in recall was only 53.3% of the maximum possible score when assessed with MoCA. In contrast, recall performance was 80.8% when assessed with MMSE. Performance in language

### Table 1. MoCA and MMSE Subtest Scores

<table>
<thead>
<tr>
<th>Subtest Details</th>
<th>Mean Raw Scores (SD) and Mean Percentage Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1 Percentage Score</td>
</tr>
<tr>
<td>MoCA subtest/max score</td>
<td></td>
</tr>
<tr>
<td>Visuoexecutive/5</td>
<td>Trail B test, cube copy, clock drawing</td>
</tr>
<tr>
<td>Naming/3</td>
<td>Confrontation naming (lion, hippo, camel)</td>
</tr>
<tr>
<td>Attention/6</td>
<td>Forward (5 digits), backward (3 digits) Tapping the letter A in letter list Serial 7 subtractions</td>
</tr>
<tr>
<td>Language/3</td>
<td>Repetition of 2 complex sentences ( \geq 11 ) words beginning with f in 1 min</td>
</tr>
<tr>
<td>Abstraction/2</td>
<td>Similarities, for example, train and bicycle=transport</td>
</tr>
<tr>
<td>Recall/5</td>
<td>Recall a list of 5 words</td>
</tr>
<tr>
<td>Orientation/6</td>
<td>Date, month, year, day, place, city</td>
</tr>
<tr>
<td>Total/30</td>
<td></td>
</tr>
<tr>
<td>MMSE subtest/max score</td>
<td></td>
</tr>
<tr>
<td>Orientation/10</td>
<td>Orientation to place and time</td>
</tr>
<tr>
<td>Registration/3</td>
<td>Repeat ball, car, man</td>
</tr>
<tr>
<td>Attention/5</td>
<td>Serial 7 subtractions World backward</td>
</tr>
<tr>
<td>Recall/3</td>
<td>Recall ball, car, man</td>
</tr>
<tr>
<td>Language/8</td>
<td>Confrontation naming (pen, watch) Repeat no ifs, ands, or buts Perform 3-step command Obey written instruction (close your eyes) Write a complete sentence</td>
</tr>
<tr>
<td>Praxis/1</td>
<td>Copy intersecting pentagons</td>
</tr>
<tr>
<td>Total/30</td>
<td></td>
</tr>
</tbody>
</table>

Mean percentage scores calculated as a percentage of maximum possible score. MMSE indicates Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; and SD, standard deviation.
was 66.7% with MoCA and 95.0% with MMSE ($P=0.001$; Figure 3). During the following 90 days, language impairments detected by MoCA remained stable at all time points (day 7, 69.4%; day 30, 68.2%; and day 90, 75.8%; $P=0.088$), but more severe than indicated by MMSE. Impairments detected by MoCA in recall, however, improved substantially from baseline to day 7 (19.5% increase; $P<0.0001$), matching MMSE scores at day 7 and onward (Figure 3).

Resolution of Cognitive Deficits

Patients with baseline impairment (n=54; MoCA<26) were then divided into 2 groups based on the improvement/worsening of cognitive function by day 30. Patients, in whom MoCA scores improved by ≥2 points by day 30, were defined as reverters (n=35; 65%). Those with persisting or worse deficits by day 30 were defined as nonreverters (n=19; 35%). Reverters improved from a baseline median (interquartile range) MoCA of 23 (7) to 27 (5) at day 30. MoCA scores in nonreverters worsened from 23 (5) to 22 (7) after 30 days.

A comparison of demographic characteristics showed that median (interquartile range) age was lower in reverters (68 [19] years) than nonreverters (79 [12] years; Tables 2 and 3). Baseline neurological deficits as assessed by NIHSS were also more common in nonreverters (14/19; 74%) than in reverters (20/35; 57%; Tables 2 and 3). Spearman correlation indicated that NIHSS scores were significantly correlated with MoCA scores at baseline ($\rho=−0.517; P=0.023$) and day 30 ($\rho=−0.514; P=0.041$) in nonreverters.

Reverters demonstrated significant improvements in all 7 subtests, with performance in the recall domain showing the greatest improvement (34% increase; $P<0.0001$). In nonreverters, 6 of 7 subtests remained the same after 30 days, whereas performance in the language domain worsened significantly (18% decrease; $P=0.045$; Tables 2 and 3).
Scores were similar in reverters (5 [7]) and nonreverters (5 [8]; \(P=0.93\)) at day 7, remained in the normal range at day 30 (reverters, 5 [11]; nonreverters, 7 [6]) and decreased by day 90 in both groups (reverters, 4 [10]; nonreverters 2 [9]; Tables 2 and 3). Spearman correlation indicated that MoCA scores were correlated with Geriatric Depression Scale scores (\(\rho=-0.316; P=0.003\)).

**Functional Outcome and Cognition**

The premorbid mRS at baseline was not significantly different between reverters (0 [0]) and nonreverters (0 [1]; \(P=0.122\)). Median mRS scores at day 30 were similar in reverters (2 [1]) and nonreverters (2 [3]). However, by day 90, these impairments resolved in reverters (0 [2]) and remained unchanged in nonreverters (2 [3]).

**Discussion**

This is the first longitudinal assessment of domain-specific cognitive impairment in patients with TIA/minor stroke, including the acute phase of the illness. The MoCA was more sensitive to language deficits, which were consistently present during the first 90 days. Memory deficits detected with MoCA at baseline improved over time. Cognitive function in patients with persisting impairment was correlated significantly with baseline neurological deficits and functional outcome.

Five studies have assessed the sensitivity of neuropsychological assessments to overall and domain-specific cognitive impairments after TIA/minor stroke.7–10,19 These studies have primarily been cross-sectional, rather than longitudinal and none assessed cognitive function after acute TIA. No previous study has used serial assessment to examine the temporal profile of domain-specific cognitive impairments after TIA/minor stroke.

Studies of the MoCA in cerebrovascular patients are consistent with our results. Pendlebury et al19 assessed 413 patients with TIA/stroke at 6-month or 5-year follow-ups using a cutoff score <26 to indicate impairment in both MoCA and MMSE. According to MoCA, 291 (70%) patients were cognitively impaired, of whom 162 (56%) had normal MMSE scores. MMSE detected impairments in only 30% of all patients. A study by Dong et al20 assessed 100 patients at a mean of 4.2±2.4 days post stroke. The MoCA detected deficits in 59% of patients, whereas only 43% were impaired according to MMSE. In another study, 91 patients were administered the MMSE and MoCA ≥1 year after TIA/stroke.4 The MoCA identified mild cognitive impairment with good sensitivity and specificity, whereas MMSE scores were consistently skewed toward higher values. The MMSE may be able to identify deficits in patients with more severe strokes.

Three cross-sectional studies have assessed domain-specific changes in cognitive function after TIA and stroke.7,9,19 Pendlebury et al19 assessed patients with TIA (n=156) or stroke (n=207) at ≥6 months after symptom onset. TIA subjects performed better than patients with stroke on 1 MMSE subtest versus 6 MoCA subtests (visuospatial tasks, attention, verbal fluency, abstraction, recall, and orientation). In patients with TIA, MoCA detected subtle deficits in recall and verbal fluency domains, which were less impaired when assessed with MMSE. In another study from the same group,
413 patients with TIA/stroke were assessed 6 months or 5 years post event. The MoCA demonstrated deficits in executive function, attention, recall, and repetition, which were not detected by the MMSE. Finally, Dong et al compared the ability of MoCA and MMSE domain subtest scores to classify cognitive patterns in 100 patients with ischemic stroke or TIA within 14 days. Based on baseline cognitive screening scores, patients were divided into 3 groups: acute vascular cognitive impairment no dementia moderate (screened positive for both MoCA and MMSE), acute vascular cognitive impairment no dementia mild (positive for either test), and no cognitive impairment (negative for both tests). The MMSE subtest scores did not differentiate between these groups, whereas MoCA subtest scores in the visuospatial/executive function, attention, and recall domains did.

Previous studies indicate that the MoCA is more difficult than MMSE, which likely improves sensitivity for mild cognitive deficits in certain domains. This is particularly relevant in the TIA/minor stroke population, where cognitive changes are subtle. To test for attention, MMSE uses only the serial 7's task, but the MoCA includes 2 additional tests (digit span and vigilance). The MoCA memory questions are more challenging, with more words, fewer learning trials, and a longer delay before recall. The MoCA also uses more tasks to assess executive function, language, and visuospatial processing thoroughly. It is likely that these differences contributed to the MoCA's higher overall sensitivity to acute impairment, as well as domain-specific changes in memory and language in our patients. The MMSE has also been associated consistently with a ceiling effect, which is the most plausible explanation for the stable MMSE scores across 90 days in our study. This ceiling effect also applied to the 5 MMSE domains (orientation, registration, attention, language, and praxis), which remained unchanged between baseline and day 90. The exception was the memory domain, which transiently worsened at day 7, improving by day 30. We do not feel that this represents a true cognitive change in our patients, as the MoCA recall scores improved. It is theoretically possible that fatigue led to worsening of performance on the MMSE, but we would expect the MoCA scores to worsen as well, unless we hypothesize a floor effect on the latter test. This is speculative, however, and this more likely represents a type I error.

Reverter status in patients with TIA/minor stroke may be explained by the presence of baseline neurological deficits. The greater severity of baseline neurological deficits observed in nonreverters may have played a role in suppressing certain cognitive domains, affecting improvement over time. It would be useful to use MRI to compare the extent of tissue injury between reverters and nonreverters. Reversion of cognitive impairment may be related to the localization of acute lesions, affecting strategic regions of cognition more so in nonreverters than in reverters.

Many of our patients had mild affective changes, which were correlated with the presence of acute cognitive changes. They did not, however, predict resolution of cognitive deficits over time. Nonetheless, an assessment of mood should also be considered in patients with most TIA/minor stroke.

This study has several limitations. We used identical versions of the MoCA test at each time point because alternate forms were not available at the time of study inception. It is possible that patients may have learned aspects of a task, contributing to the development of a learning curve. Modifying details of certain tasks such as recall words and repetition sentences would help minimize learning effects. In addition, although patients with preexisting dementia were excluded, it is possible that some patients with stroke with mild cognitive impairment without dementia (vascular cognitive impairment no dementia) may have gone undetected and therefore influenced results. Cognitive assessment timing (time of day/beginning versus end of the visit) and fatigue may have also resulted in decreased capacity to sustain an effort, increasing the likelihood of error. Finally, language barriers may have hindered the patient's ability to thoroughly understand certain tasks, contributing to increased error.

Conclusions
An MoCA is the preferred cognitive screening test in patients with TIA/minor stroke. Given the frequency of cognitive changes seen in this population, it could be considered a standard assessment tool. The transient cognitive changes seen in some patients suggest that studies of long-term cognitive changes after stroke/TIA should include a baseline assessment at day 90 or later, after acute changes have stabilized. Persisting cognitive deficits are relevant, as they are correlated with functional outcome. These findings are relevant to patients with TIA/minor stroke disposition and advice with respect to vocation, driving, and activities of daily living.

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Disclosures
None.

References
9. Dong Y, Sharma VK, Chan BP, Venkatesubramanian N, Teoh HL, Seet RC, et al. The Montreal Cognitive Assessment (MoCA) is superior to the

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Mini-Mental State Examination (MMSE) for the detection of vascular cognitive impairment after acute stroke. *J Neurol Sci.* 2010;299:15–18.


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