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Can we forget the Mini-Mental State Examination? A systematic review of the validity of cognitive screening instruments within one month after stroke

Caroline M Van Heugten1,2, L Walton1 and U Hentschel1

Abstract
Objective: To review systematically studies investigating the convergent, criterion, and predictive validity of multi-domain cognitive screening instruments in the first four weeks after stroke.

Data sources: Electronic databases (Pubmed, PsycINFO, CINAHL, Embase) were searched until June 2014.

Review methods: Studies concerning screening for cognitive dysfunction in stroke patients using multi-domain instruments, within four weeks postinfarct or haemorrhagic stroke, using tests taking no longer than one hour. Convergent, criterion, and predictive validity were examined.

Results: A total of 51 studies investigating 16 cognitive screening instruments were identified. None of the instruments covered all of the most affected cognitive domains. Only one study investigated the convergent validity of a multi-domain test during the (sub)acute phase after stroke. A total of 15 studies examined the criterion validity of cognitive measurements during the acute phase after stroke. The Montreal Cognitive Assessment and Higher Cortical Function Deficit Test had good criterion validity. A total of 24 studies examined the predictive ability of multi-domain cognitive instruments applied in the acute phase after stroke. The Cognistat, Montreal Cognitive Assessment, and Functional Independence Measure-cognitive showed good predictive validity. The Mini-Mental State Examination is the most widely used cognitive screening instrument, but shows insufficient criterion validity.

Conclusion: None of the existing instruments fulfils all criteria. The Montreal Cognitive Assessment is the best candidate at present, provided items measuring speed of information processing are added, and further studies investigating the optimal cut-offs are conducted.

Keywords
Stroke, cognition, acute management

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Introduction

Cognitive deficits occur in up to 80% of patients who have suffered a stroke.\textsuperscript{1,2} Impairments in all cognitive domains are included, but the domains most commonly afflicted are visuo-spatial abilities, executive functions, memory, and speed of information processing.\textsuperscript{3,4} These cognitive deficits can have negative consequences for daily living, quality of life, and return to work.\textsuperscript{5,6} Also, cognitive symptoms place a large burden on caregivers\textsuperscript{7} and are associated with post-stroke depression in the chronic phase.\textsuperscript{8}

Given this impact, identifying cognitive deficits in the first days or weeks after stroke is essential for planning the most appropriate rehabilitation treatment, the discharge destination, and for discussing problems the patients and relatives may encounter in future. Many stroke guidelines recommend cognitive screening early after stroke, which has even been denoted a quality marker for stroke services.\textsuperscript{9}

Extensive neuropsychological assessment examining all cognitive domains separately and thoroughly is not feasible early after stroke, because patients may not be medically stable or arousal levels and fatigue can confound the findings. Nevertheless, domain-specific cognitive abilities have a high prognostic value for cognitive and functional outcome.\textsuperscript{10}

Screening measures need to be efficient. They should: test at least the most affected domains after stroke; be sufficiently sensitive to detect those patients with cognitive problems; correlate with cognitive measures testing the same domains; and have predictive value for functional outcome.

Many screening instruments were developed to identify people with dementia and are therefore sensitive to memory deficits but not to other cognitive deficits commonly seen after stroke. The Mini-Mental State Examination (MMSE) is the most widely used instrument, but it has insufficient sensitivity to detect patients with cognitive deficits after stroke.\textsuperscript{11,12}

The National Institute of Neurological disorders and Stroke (NINDS) proposed harmonizing screening for cognitive impairment on the basis of network discussions.\textsuperscript{9} Therefore, we have systematically reviewed studies using a multi-domain cognitive screening instrument in the first four weeks after stroke. The main questions reviewing these instruments were: (1) which instruments have been employed to measure cognitive assessment during (sub)acute stroke; (2) which of these instruments has the best convergent validity; (3) which instrument has the best criterion validity in terms of sensitivity and specificity; and (4) which instrument has the best predictive validity?

Methods

Protocol and registration

The review protocol was not registered.

Eligibility

A systematic search was performed to identify potential tools. Our inclusion criteria were: (1) studies investigating stroke patients who had suffered cerebral infarct or haemorrhage; (2) assessment of cognitive functioning; (3) during the (sub)acute phase, i.e. less than four weeks post-stroke; (4) by using a multi-domain (i.e. more than two cognitive domains) screening instrument; (5) shorter than one hour of testing (i.e. the time needed to screen should be mentioned in the article or should be known for the particular instrument on the basis of other sources). Articles in which one or more of these criteria could not be checked because of lack of information, were not selected for further use.

Information sources

We searched four databases: Pubmed, PsycINFO, CINAHL, and Embase.

Search

There were no limitations in terms of publication date. The final search was done on 25 June 2014. Studies were filtered for humans, >18 years of age. Studies written in English, Dutch, German, French, or Swedish were selected. Appendix 1 (available online) displays the search terms and the Pubmed strategy that was used.
Study selection

The initial search was done until December 2011. All studies were selected by two authors (LW and UH) independently. In case of disagreement, the first author (CvH) was addressed to resolve the issue. In doing so, an agreement of 92% was obtained over all studies. The update of the search until June 2014 was done by the first author, because agreement in the initial search was high. To ensure that no studies were missed via the search platforms, cross-referencing was applied to the final set of articles.

Data collection process

Data extraction sheets were made and filled by the authors. The articles were divided among the authors. In case of doubt about information, all authors checked the same article.

Data items

To describe the instruments, the following characteristics were extracted: name of the instrument, number of items, domains tested, cut-off values, and score range. Studies reporting the prevalence of cognitive deficits are described in terms of number of participants, time since stroke, test used, cut-off value, and percentage of patients impaired. Convergent validity is described in terms of the test of interest and the comparator variables. For the criterion validity sensitivity and specificity are reported. The predictive validity is presented in terms of the predictor variable of interest, the outcome variables.

Summary measures

Convergent validity refers to the extent to which the screening instrument corresponds to similar instruments measuring cognitive functioning and is expressed in correlations. Criterion validity refers to the extent to which the test results of the screening instrument are comparable with the results of a criterion measure and was considered sufficient if sensitivity (i.e. percentage of patients correctly classified as cognitively impaired) was higher than 80% and specificity (i.e. percentage of patients correctly classified as not impaired) was higher than 60%. In this article, predictive validity refers to the extent to which the screening instrument can predict outcome measures, such as cognitive functioning or functional outcome. For the predictive validity, B-values or odds ratios are presented.

Results

In Figure 1 a flowchart of the selection process is presented. The selection process led to a total of 51 articles to be included in our study. In total 16 screening instruments were reviewed.

Test characteristics

There were 16 multi-domain cognitive tests used in the 51 studies. The instruments are presented in Table 1. Unfortunately, not all necessary information to appraise each instrument fully is available, such as cut-off scores and score range.

No instrument assesses all of the most commonly affected cognitive domains after stroke, i.e. speed of processing, memory, executive functioning and visuospatial abilities. The Montreal Cognitive Assessment (MoCA) approaches this criterion assessing memory, visuospatial abilities and executive functioning. Other tests, such as the Addenbrooke’s Cognitive Examination Revised (ACE-R), the Comprehensive Cognitive
### Table 1. Cognitive screening instruments.

<table>
<thead>
<tr>
<th>Test name</th>
<th>Total number of items</th>
<th>Domains tested (subtests)</th>
<th>Cut-off score</th>
<th>Score range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addenbrooke's Cognitive Examination Revised (ACE-R)</td>
<td>26</td>
<td>5 subscales: attention/orientation (4), visuospatial (5), fluency (2), memory (5), language (10)</td>
<td>Different scores used: 75, 82, 88 (yielding at different sensitivity and specificity values; best 82)</td>
<td>0–100</td>
</tr>
<tr>
<td>Abbreviated Mental Test-4 (AMT-4)</td>
<td>4</td>
<td>Cognitive impairment</td>
<td>3/4</td>
<td>0–4</td>
</tr>
<tr>
<td>Abbreviated Mental Test-10 (AMT-10)</td>
<td>10</td>
<td>6 subscales: speech quality (4), language (16), auditory comprehension (4), ideomotor apraxia (34), ideational apraxia (8); visuospatial-constructive (14)</td>
<td>7/8</td>
<td>0–10</td>
</tr>
<tr>
<td>Assessment of Stroke and other Brain damage (ASB)</td>
<td>80</td>
<td>6 subscales: speech quality (4), language (16), auditory comprehension (4), ideomotor apraxia (34), ideational apraxia (8); visuospatial-constructive (14)</td>
<td>3 score levels: High (157–160) Medium (32–148) Low (0–23)</td>
<td>0–160</td>
</tr>
<tr>
<td>Comprehensive cognitive neurological test in stroke (COCONUTS)</td>
<td>60</td>
<td>8 subscales: general attentional systems (2); left hemisphere network for language, Gerstmann’s, Angular gyrus syndrome (13); hippocampal limbic network for memory and emotion (4); prefrontal network, subcortical network for executive function and comportment (9); dorsal right parieto-frontal network for visuo-spatial function, attention, emotion and prosody (10); ventral occipito-temporal network for object and face recognition (12); syndromes with ill-defined neural networks (5); miscellaneous syndromes (5)</td>
<td>Mean +1 SD is abnormal for: memory, frontal, attention and concentration, visuospatial, complex visual processing Any error is abnormal for: orientation, language, praxis, emotion, neglect, anosognosia, prosody and delusional misidentification syndrome</td>
<td>0–116</td>
</tr>
<tr>
<td>Cog-4 (National Institute of Health Stroke Scale)</td>
<td>4</td>
<td>4 items: orientation, ability to follow commands, language and inattention</td>
<td>0–9</td>
<td>&gt;0</td>
</tr>
<tr>
<td>Cognistat since 1995 (<a href="http://www">www</a>. cognistat.com); Neurobehavioral Cognitive Status Examination (NCSE) before 1995</td>
<td>Not available</td>
<td>10 subtests: orientation, attention, language (comprehension, repetition, and naming), constructional ability, memory, calculation, and reasoning (similarities and judgment)</td>
<td>no sum score</td>
<td>range per subtest</td>
</tr>
<tr>
<td>Functional Independence Measure-cognitive subscale (FIM-cog)</td>
<td>5</td>
<td>2 subscales: communication (2), social cognition (3)</td>
<td>3 score levels: No helper required (6–7) Helper/modified dependence (3–5) Helper/complete dependence (0–2)</td>
<td>5–35</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*Note: Different scores used: 75, 82, 88 (yielding at different sensitivity and specificity values; best 82).*

*Note: Mean +1 SD is abnormal for: memory, frontal, attention and concentration, visuospatial, complex visual processing Any error is abnormal for: orientation, language, praxis, emotion, neglect, anosognosia, prosody and delusional misidentification syndrome*
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</tr>
</thead>
<tbody>
<tr>
<td>Higher Cortical Function Deficit Tests (HCFT)²²</td>
<td>55</td>
<td>9 subscales: aphasias (8), anosognosias and neglect syndromes (5), frontal network syndromes (3), amnesias (4), apraxias (7), alexias (3), agnosias (5), visuospatial dysfunction/constructional apraxia (1), aprosodias (3), miscellaneous group (16)</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>Loewenstein Occupational Therapy Cognitive Assessment (LOTCA)²³ (<a href="http://www.lotca.com">www.lotca.com</a>)</td>
<td>20</td>
<td>4 subscales: orientation (2), visual and spatial perception (6), visuomotor organization (7), thinking operations (5)</td>
<td>4 score levels: 1: Patient fails to perform the task; 2: Patient is able to perform part of the task; 3: Patient is able to perform most of the task; 4: Patient demonstrates good performance of the task</td>
<td>20–83</td>
</tr>
<tr>
<td>Mindstreams™ computerized cognitive assessment²⁴</td>
<td>Not available</td>
<td>Verbal memory, non-verbal memory, go-no go, stroop, visual spatial imagery, verbal rhyming, staged information processing, problem solving, ‘catch’ game</td>
<td>Not available for stroke</td>
<td>Automatized conversion of raw scores into index scores and global functioning scores; ranges not available</td>
</tr>
<tr>
<td>Mini-Mental State Examination (MMSE)²⁵</td>
<td>30</td>
<td>Orientation, attention, learning, calculation, delayed recall, construction</td>
<td>Different cut-off scores; standard 23/24</td>
<td>0–30</td>
</tr>
<tr>
<td>Modified Mini-Mental State Examination (3MS)²⁶</td>
<td>34</td>
<td>Cognitive impairment</td>
<td>79/80</td>
<td>0–100</td>
</tr>
<tr>
<td>Montreal Cognitive Assessment (MoCA)²⁷ (<a href="http://www.mocatest.org">www.mocatest.org</a>)</td>
<td>30</td>
<td>Visuo-executive, naming, attention, language, abstraction, delayed recall, orientation</td>
<td>Different cut-off scores; standard 25/26</td>
<td>0–30</td>
</tr>
<tr>
<td>Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)²⁸²⁹ (<a href="http://www.rbans.com">www.rbans.com</a>)</td>
<td>12</td>
<td>5 subscales: immediate memory (2), visuospatial/constructural (2), language (2), attention (2), delayed memory (4)</td>
<td>Different cut-off scores; 85 (= -1 SD); 77.5 (= -1.5 SD)</td>
<td>5 index scores and total score each with mean value of 100 (SD = 15)</td>
</tr>
<tr>
<td>Screening Instrument for Neuropsychological Impairment in Stroke (SINS)²⁰</td>
<td>18</td>
<td>3 subscales: aphasia (4), apraxia (8), visuo-cognitive (6)</td>
<td>Cut-offs for subscales: 14–54</td>
<td>4–12 (aphasia); 8–24 (apraxia); 6–18 (visuo-cognitive)</td>
</tr>
<tr>
<td>Short Portable Mental Status Questionnaire (SPMSQ)³¹</td>
<td>10</td>
<td>Orientation, remote memory, concentration</td>
<td>More than 4 errors</td>
<td>0–10</td>
</tr>
</tbody>
</table>
Neurological Test in Stroke (COCONUTS), the Cognistat, the Higher Cortical Function Deficit Test (HCFD), the MMSE, and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) measure only two of these domains.

Some instruments have preferred cut-off values, such as 23/24 for the MMSE,32–36 while one study used the mean minus two standard deviation of a norm group37 and one study tried to integrate three cut-off values.38 The preferred cut-off value for the MoCA is either 26 or 27.35,36,39–41

Four studies applied a short neuropsychological battery instead of one instrument.4,42–44 One study used the 3MS, the modified version of the MMSE.45

**Convergent validity**

Only one study investigated the convergent validity of a multi-domain test during the (sub)acute phase after stroke.46 Strong significant inter-correlations were found between the Loewenstein Occupational Therapy Cognitive Assessment (LOTCA), the MMSE, and the Functional Independence Measure Cognitive subscale (FIM-cog).

In only two studies, different cognitive screening instruments were correlated to assess the convergent validity of the Cog-441 and the Mindstreams™ global score.47 Three of the four Cog-4 domains (i.e. orientation, language, and inattention)41 and the Mindstreams™ global score47 correlated significantly with the MoCA, but the Cog-4 domain executive functioning did not.41

Other studies correlated the findings of a certain instrument with other present or future variables that are of interest in neurorehabilitation and are often found to be associated with cognitive functioning. The results in Table 2 (available online) display that the MMSE was applied three times out of the eight associative studies.32,46,48 This test correlated significantly with the patients’ perceived satisfaction concerning their functional outcome measurements at six months48 and the functional outcome measure itself.32,46 Three of the Cog-4 items41 and the Mindstreams™ global score47 correlated significantly with the MoCA.

The Short Portable Mental Status Questionnaire (SPMSQ) correlated strongly and significantly with neurological measurements in the acute phase,49 and the Cognistat was correlated significantly with both functional and mood measurements.50 Furthermore, the Abbreviated Mental Test51 showed a significant correlation with functional outcome and mood measures at a follow-up of six months. The Functional Independence Measure Cognitive subscale was also associated with functional outcome,32 though a comparison study between the LOTCA, MMSE, and FIM-cog by Zwecker et al.46 displayed the LOTCA to have the strongest correlation with functional outcome.

**Criterion validity**

A total of 15 studies studied the criterion validity of cognitive measurements during the acute phase after stroke (Table 3, available online). By applying the sensitivity/specificity criterion (i.e. 80%/60%) three instruments remained: MMSE, MoCA, and the HCFD.

First, the MMSE received adequate sensitivity and specificity scores in two studies by Dong and colleagues.52,53 However, all other studies examining the criterion validity of the MMSE did not duplicate this finding.13,54–56 One study12 evaluated all possible cut-off scores for the MMSE and the authors concluded that no cut-off score could accomplish a good sensitivity and specificity. The second instrument with good criterion validity was the MoCA. Five studies regarded it as conforming to our criterion39,36,52,53,57 and it only slightly falls short in a study by Godefroy et al.56 (sensitivity: 78% and specificity: 90%). Finally, Hoffmann and colleagues assessed two multi-domain tests. The HCFD gained good criterion validity,22 though was only applied once, while the COCONUTS did not fulfil our criterion.58

The Screening Instrument for Neuropsychological Impairment in Stroke (SINS) did not calculate a total sensitivity and specificity score.59 However, the three subtests, i.e. aphasia, visuo-constructive, and apraxia subscales, all displayed good criterion validity.
Predictive validity

A total of 24 studies examined the predictive ability of multi-domain cognitive instruments applied in the acute phase after stroke (Table 4, available online). The outcome measures to be predicted were cognitive functioning (eight times), functional outcome (11 times), mood (three times), length of stay (one time), and level of caregiver assistance (one time). Mostly, the cognitive screening instrument was used to predict future functioning either defined in terms of time or specific event such as discharge. Only two studies used regression analyses to predict cognitive functioning or depressive symptoms at the same time point. Ten different tests were applied to predict these outcome measurements, i.e. MMSE (13 times), Cognistat (three times), FIM-cog subscale (two times), a neuropsychological battery (two times), Abbreviated Mental Test (two times), MoCA (three times), and Assessment of Stroke and other Brain Damage (ASB) (one time).

The MMSE was applied in 13 studies and has been employed to predict mood, cognition, and functional outcome. However, the results are mixed, with studies demonstrating both significant and non-significant findings of the MMSEs predictive ability. The MoCA was recently used three times and could significantly predict long term cognitive impairment but for functional outcome the results were mixed. The Cognistat was employed three times and could significantly predict functional outcome, though Gillen and colleagues did not confirm these findings. The FIM-cog was used twice and significantly predicted level of caregiver assistance, though was not able to predict cognitive functioning of stroke patients. Also, two studies displayed the Abbreviated Mental Test to significantly predict functional outcome and depressive symptoms.

Other tests showing good predictive values were the RBANS and the ASB. These tests could significantly predict functional outcome, though they were only applied once.

A selection of neuropsychological tests was administered in three studies to predict future cognitive impairments. The neuropsychological battery proposed by Nys et al. and the working memory domain used by Jaillard et al. could significantly predict cognitive functioning at follow-up, while the tests chosen by Prescott et al. did not predict cognitive functioning.

Discussion

Our review found 16 measures have been used to screen for cognitive deficits in the first four weeks after stroke. None of these 16 instruments fulfilled all criteria for cognitive screening in the acute phase after stroke, but the MoCA seems to be the best candidate so far and has recently been used most often. None of the instruments, including the MoCA, measured all most affected cognitive domains. However, the label for a cognitive domain is different in the various instruments. Therefore, similar labels might be tapping into different cognitive domains or different labels might actually measure the same domain.

A critical note related to this review should be made: One could question the need for cognitive screening after stroke. Screening suggests that there are patients with and patients without cognitive deficits and that distinguishing is necessary. Given the high prevalence of cognitive deficits, it may be better to assume that deficits are present. For the more severe stroke patients, cognitive deficits are obvious and screening is not necessary; for the mild strokes it becomes more and more clear that, despite ‘good recovery’, many patients show multi-domain cognitive impairments that can impact return to life as before the stroke. Van Dijk and de Leeuw explain that the best way to recognize cognitive dysfunctioning is to simply look for it, beyond the more plausible factors to look for, such as walking and talking.

Cognitive screening is useful in older adults when screening for cognitive impairments because these may be missed by primary care clinicians in a routine check-up. In a recent review on cognitive screening instruments in older adults, 12 brief instruments could be identified that were used more than once in well-designed diagnostic accuracy studies. The MMSE was used most (in 25 of the 55 studies) and appeared to have good diagnostic accuracy in this group: 88.3% sensitivity and 86.2%
specificity. This is, however, not surprising since the instrument was designed for this purpose.

When combining the different properties, the widely used, popular MMSE does not come out positively in stroke research. It estimates cognitive abilities to be present to a much lesser extent than other instruments and portrays mixed results in its predictive ability. Also, the majority of studies concerning its criterion validity reveal the MMSE to especially have a low sensitivity; letting patients with cognitive deficits go unnoticed when in need of cognitive rehabilitation. Furthermore, the MMSE does not test the most commonly affected cognitive domains after stroke and studies do not agree on one cut-off score. For these reasons, it seems advisable to dissuade using the MMSE in a population of stroke patients during the (sub)acute phase.

This review further revealed that studies are difficult to compare, even when type of stroke and time since stroke are similar, because different cut-off values are used for the same instrument and for some instruments cut-off scores or maximum scores are not even available. Other instruments might be potential candidates for future use, but have only been used occasionally until now. The question is whether the currently available instruments should be optimized further or whether there is still a need to develop new instruments.

In every systematic review one has to consider whether valuable and relevant studies have been missed. Since cross-referencing did not lead to the inclusion of further studies, we believe our conclusions can be drawn on the most important studies to be found in the literature. However, the language filter may have caused a selection bias. Furthermore, the heterogeneity of the study methods did not permit the performance of a meta-analysis. Furthermore, we choose to examine some psychometric properties that we thought to be most relevant to the goal of the study; other aspects of the instruments could raise additional information. Studies with patients who had suffered a subarachnoid haemorrhage, transient ischemic attack, or lacunar stroke were excluded from this review, as were studies with mixed brain injury samples. This was done in order to study a homogeneous population in terms of aetiology and care delivered. In clinical practice, however, these groups are often mixed and cognitive screening may be done equally in these groups.

In conclusion, on the basis of the current information, the MoCA is recommended for cognitive screening in patients within four weeks after stroke, while it is advisable to remove the MMSE from standard screening batteries in clinical practice. The MoCA should be accompanied or extended with measures of speed of information processing. Further research is necessary to raise optimal cut-off values for screening purposes.

### Clinical messages

- At present, the Montreal Cognitive Assessment (MoCA) is the best candidate for cognitive screening in stroke patients.
- The Mini-Mental State Examination (MMSE) shows insufficient criterion and predictive validity in stroke patients and should not be used for screening purposes.

### Conflict of interest

The authors declare that there is no conflict of interest.

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