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Restrictions of the Mini-Mental State Examination in acute stroke

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Abstract

While the Mini-Mental State Examination (MMSE) was originally developed to screen for dementia and delirium, many neurologists use this measure as a screening instrument for 'cognitive impairment' in hospitalized stroke patients. However, the validity of the MMSE as such has never been evaluated in acute stroke. We administered the MMSE in addition to a neuropsychological examination covering six cognitive domains to 34 stroke patients (mean interval between stroke and examination, 6.5 ± 2.9 days) and 34 healthy controls. The area under the receiver operating characteristic curve (AUC) was calculated in addition to the sensitivity and specificity for various cut-off points on the MMSE.

Seventy percent of the patients were impaired in at least one cognitive domain. The accuracy of the MMSE in detecting cognitive impairment was no better than chance (AUC = 0.67; $p = 0.13$). No optimum MMSE cut-off value could be identified. The MMSE is particularly insensitive to impairments in abstract reasoning, executive functioning, and visual perception/construction.

Keywords: Mini-Mental State Examination (MMSE); Stroke; Construct validity; Neuropsychological assessment

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1. Introduction

Cognitive disorders in the acute stage of stroke are common and are important independent predictors of adverse outcome in the long term (Nys et al., 2005). Therefore, a whole range of brief cognitive measures has been used to screen for cognitive impairment in patients with acute stroke. The Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) is currently the mainstay of screening instruments. This instrument was originally developed to screen for dementia and delirium in a psychiatric setting, and has been shown to have a good sensitivity and specificity as such (Folstein et al., 1975). Subsequently, the use of the MMSE has been extended and many studies now use it as a screening instrument for ‘global cognitive impairment’ (e.g. Narushima, Chan, Kosier, & Robinson, 2003; Patel et al., 2003). However, the validity of the MMSE as a cognitive screening instrument has been questioned in both neurological and psychiatric patients (Grace et al., 1995; Faustman, Moses, & Csernansky, 1990). Moreover, there is no consensus in the cut-off values that are applied to discriminate between cognitively intact and impaired patients.

Blake and co-workers recently investigated the sensitivity and specificity of the MMSE as a screening tool for post-stroke cognitive impairment (Blake, McKinney, Treece, Lee, & Lincoln, 2002). They compared performance on the MMSE in the early stage of stroke with performance on a neuropsychological examination that was administered within 3 months of the screening assessment. The sensitivity of the MMSE when applying a cut-off value of 24 was found to be moderate (62%). However, given that there was a very large inter-individual variation in the test interval and that the degree of cognitive recovery is greatest in the first months post-stroke (Lezak, Howieson, & Loring, 2004), their methodology may have resulted in an overestimation of the sensitivity of the MMSE in initially impaired patients who had recovered by the time of the neuropsychological examination. In addition, as the authors pointed out, not all patients completed the neuropsychological examination.

The aim of the present study was to evaluate the construct validity of the MMSE as a screening instrument for cognitive impairment in patients with acute stroke. The MMSE and a full neuropsychological examination covering 6 cognitive domains was administered within 2 weeks post-stroke, and the diagnostic sensitivity and specificity of the MMSE was examined. Moreover, we evaluated which cognitive deficits were most often disregarded by the MMSE.

2. Methods

2.1. Participants

2.1.1. Patients

The population consisted of 38 consecutive acute stroke patients admitted to stroke units of two hospitals in the Netherlands (Tweesteden Hospital and St. Elisabeth Hospital Tilburg). Eligible patients were patients with either ischemic stroke or primary intracerebral hemorrhage. The diagnosis of stroke was based on the presence of both an acute focal deficit and an associated lesion on CT or MRI. Exclusion criteria for this study were a high degree of handicap

Table 1
Patient and control characteristics ($N = 34$ for each group)

	Patients	Controls	*p*-value
Demographics			
Age, mean ± S.D.	64.7 ± 11.5	65.7 ± 12.0	0.7
Male sex (%)	41.2	41.2	1.0
Education, median (range)[a]	4 (1–7)	4 (2–7)	0.2
Handedness, right (%)	88.2	85.3	0.5
Degree of handicap			
Modified Rankin Scale, median (range)	3 (1–4)		
Pre-existent cognitive functioning			
IQ-code	3.3 ± 0.4		
Oxford Community Stroke Project			
LACI	21		
PACI	5		
POCI	6		
TACI	1		
POCH	1		
Recurrent stroke, *n*	14		
Lesion side, *n*			
Right	17		
Left	17		

Abbreviations: LACI, lacunar infarct; PACI, partial anterior circulation infarct; POCI, posterior circulation infarct; TACI, total anterior circulation infarct; POCH, posterior circulation hemorrhage.

[a] Education level is scored using 7 categories (1 = not finished primary school; 7 = university degree).

(modified Rankin Scale > 4) ($N = 1$), non-native speaker ($N = 1$), and severe disturbances in communication and consciousness ($N = 1$). One patient was blind (pre-existent impairment) and therefore was not included in this study. This resulted in a study population of 34 stroke patients.

2.1.2. Controls

A control group was assembled as a reference sample for the neuropsychological examination, consisting of 34 subjects living in the community. The controls were volunteers who came to our attention through advertising in newspapers or by word of mouth. Control subjects were carefully matched to the stroke patients with respect to age, education, gender and handedness (Table 1).

2.2. Procedure

2.2.1. Demographics

Basic demographic information was collected including age, sex, handedness, and level of education. Level of education was scored according to a Dutch classification system consisting of seven categories ranging from 1: primary school not finished, to 7: university degree obtained (Nys et al., 2005). Patient and control characteristics are presented in Table 1.

2.2.2. Stroke characteristics

An experienced stroke neurologist classified strokes according to the Oxford Community Stroke Project (OCSP) classification (Bamford, Sandercock, Dennis, Burn, & Warlow, 1991), which is a simple clinical scheme to subdivide acute strokes. Patients may be classified by using clinical criteria only, although we did have CT or MRI scans available to differentiate ischemic and hemorrhagic stroke types. Subtypes of the OCSP are lacunar infarct/hemorrhage (LACI/LACH), partial anterior circulation infarct/hemorrhage (PACI/PACH), total anterior circulation infarct/hemorrhage (TACI/TACH), and posterior circulation infarct/hemorrhage (POCI/POCH). The side of the stroke lesion and history of stroke were also noted. The modified Rankin Scale was used to measure the patients' degree of handicap (van Swieten, Koudstaal, Visser, Schouten, & van Gijn, 1988). The scale consists of 6 grades, from 0 (no symptoms) to 5 (severe disability).

2.2.3. Neuropsychological examination

The mean interval between the stroke event and the neuropsychological examination was 6.5 ± 2.9 days (range 2–14). Each patient underwent the MMSE and in the same session a detailed neuropsychological examination lasting 1.5 h entailing the following cognitive domains (Lezak et al., 2004): (1) abstract reasoning [Raven Advanced Progressive Matrices (short form) and Similarities (WAIS-III)], (2) verbal memory [Rey Auditory Verbal Learning Test and Digit span WAIS-III], (3) executive functioning [Letter fluency, the Brixton Spatial Anticipation Test, which is a measure of strategic switching and problem-solving that does not require a verbal response (Burgess & Shallice, 1997), and the Visual Elevator (Test of Everyday Attention: Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994)], in which patients have to count up an down as they follow a series of visually presented floors in an elevator; this test assesses cognitive flexibility, (4) visual perception and construction [Judgement of Line Orientation (short form), Test of Facial Recognition (short form), Rey-Osterrieth Complex Figure–copy], (5) visual memory [Corsi Block span and Rey Complex Figure Delay], and (6) language [Token Test (short form) and Boston Naming test (short form)]. The short Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE Dutch Version) (de Jonghe, Schmand, Ooms, & Ribbe, 1997) was administered as a measure of pre-existent cognitive functioning. This questionnaire is a homogenous rating scale, which asks an informant about changes in the patients' everyday cognitive function.

2.3. Statistical analysis

Patients' neuropsychological test results were standardized into *z*-scores, based on the means and standard deviations of the control group. Next, we created cognitive domain scores by averaging *z*-scores of tasks belonging to the same cognitive domain. Cut-off scores for cognitive impairment within each domain were determined for a performance that differed from the control mean at the 0.05 level of statistical significance (z-score < -1.65) (Clark-Carter, 1997).

Patients without a deficit in one of the cognitive domains were considered to be cognitively intact.

Pearson or Spearman correlation coefficients were calculated between the MMSE score and (1) age, (2) education level, and (3) IQ-code. The area under the receiver operating characteristic curve (AUC) was calculated for the MMSE in relation to the presence of overall cognitive impairment as assessed with the neuropsychological examination. The AUC can vary between 0.5 and 1. The ideal test has an AUC of 1, meaning 100% sensitivity and specificity. The sensitivity and the specificity for various cut-off points of the MMSE were determined (sensitivity = true positives/true positives + false negatives; specificity = true negatives/true negatives + false positives). When evaluating the usefulness of a screening measure to identify those individuals with cognitive impairment, a good sensitivity (>80%) is required, while maintaining an acceptably low false positive rate (specificity > 60%) (Blake et al., 2002).

3. Results

Three healthy controls (8%) demonstrated a cognitive deficit in at least 1 cognitive domain. More specifically, 1 control subject (3%) demonstrated a deficit in abstract reasoning, 2 controls (6%) in verbal memory, and 2 controls in language (6%), whereas no impairments were found in executive functioning, visual perception/construction, or visual memory. Overall, 70% of patients were impaired in at least 1 cognitive domain as assessed with the neuropsychological examination. More specifically, 47% of patients demonstrated an impairment in abstract reasoning, 32% showed an impairment in executive functioning, 26% in language, 21% in visual perception and construction, 15% in verbal memory, and 12% in visual memory. The prevalence of patients with cognitive impairment according to the MMSE is shown in Table 2. The median score on the MMSE was 24 (range 14–30). There was no significant correlation between the MMSE score and the age of patients ($r = -0.14$, $p > 0.05$), education level ($r = 0.28$, $p > 0.05$), or pre-existent level of cognitive functioning (IQ-code) ($r = 0.02$, $p > 0.05$).

When differentiating patients with cognitive impairment from cognitively intact patients, the MMSE had an AUC of 0.67 (standard error = 0.11), indicating that the MMSE performed

Table 2
Sensitivity and specificity of the MMSE

MMSE cut-off	Sensitivity (%)	Specificity (%)	Prevalence of cognitive impairment according to MMSE (%)
<23	30.4	100	23.5
<24	34.8	70	35.3
<25	56.5	60	52.9
<26	69.6	40	67.6
<27	95.7	40	85.3
<28	100	40	88.2
<29	100	30	91.2

Grey areas indicate acceptable sensitivity (>80%) or specificity (>60%).

statistically no better than chance ($p = 0.13$). The sensitivity and specificity of the MMSE is presented in Table 2. No optimum cut-off scores yielding both a sensitivity greater than 80% and a specificity greater than 60% could be identified.

When applying a cut-off value of 24, which is a frequently used cut-off value for hospitalized patients, 11 of the 16 patients (69%) with reasoning disturbances in the early phase of stroke were misclassified as cognitively intact by the MMSE, as were 7 of the 11 patients (64%) with executive disorders, 4 of the 7 patients (57%) with visual perceptual impairments, 2 of the 4 patients (50%) with visual memory deficits, 4 of the 9 patients (44%) with language disorders, and 1 of the 5 patients (20%) with verbal memory disorders.

4. Discussion

The present study shows that the MMSE is an invalid screening tool to discriminate between cognitively intact and impaired patients with acute stroke. Before we interpret our findings, it should be noted that the majority of patients in our sample included patients with subcortical lacunar stroke. Nevertheless, 70% of this population demonstrated cognitive impairment, which may in part have been caused by a previous stroke, and our study shows the insensitivity of the MMSE to detect cognitive impairment as such. Our findings are in contrast with the good sensitivity and specificity that has been reported when the MMSE is used as a screening tool for dementia (Folstein et al., 1975). Prior studies have reported other limitations of the MMSE such as insensitivity to right-hemisphere lesions (Dick et al, 1994; Grace et al., 1995), mild cognitive disturbances (Schwamm, Van Dyke, Kiernan, Merrin, & Mueller, 1987), and amnesia (Benedicte & Brandt, 1992). While most studies adopt a cut-off value of 24 to indicate impaired cognition in stroke patients, our findings show that the sensitivity of the MMSE is extremely poor when using this value (34.8%). Consequently, in a majority of cognitively disturbed patients, impairments may not be taken into account in planning both discharge destination and rehabilitation trajectory. Cognitive disorders that are most often disregarded by the MMSE in acute stroke patients are impairments in more complex cognitive functioning such as abstract reasoning and executive functioning, but also in visual perception and construction. Given that our findings also show that impairments in reasoning and executive functioning are the most frequent cognitive impairments in the early phase post-stroke, the MMSE should be interpreted with caution when used as a screening instrument for cognitive impairment in patients with acute stroke.

In an ongoing large-scale longitudinal study, we are examining the nature and prevalence of specific cognitive disorders in acute stroke patients and the recovery patterns associated with these cognitive disorders. This may elaborate our understanding in the nature of impairments in these patients and perhaps in the development of a stroke-specific cognitive screening instrument. Moreover, during the last couple of years several new screening instruments have been developed which incorporate items that assess executive functioning and reasoning, e.g. the CAMCOG (de Koning et al., 1998), and the seven minute screen (7MS) (Meulen et al., 2004). The sensitivity and specificity of these instruments remains to be determined in acute stroke, but it is likely that these measures are more appropriate than the MMSE in detecting post-stroke cognitive impairment.

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