Screening for post-stroke neurocognitive disorders in diverse populations: A systematic review

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Abstract

Objective: Although neurocognitive disorders (NCD) are common post-stroke, many populations do not have adapted cognitive screens and cut-offs. We therefore reviewed the appropriateness of the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Oxford Cognitive Screen (OCS) for diagnosing NCD in culturally diverse stroke populations.

Method: Using an extensive search string, diagnostic accuracy studies for MMSE, MoCA and OCS in the stroke population were retrieved from four databases. We compared translations and adaptations, adjustments in scores and cut-offs, and their diagnostic accuracy.

Results: The search resulted in 28 MMSE, 39 MoCA and 5 OCS-studies in 13 western, educated, industrialized, rich and democratic (WEIRD) and 4 other countries. There was a lack of studies on South-American, African, and non-Chinese-Asian populations. All three tests needed adaptation for less WEIRD populations and populations with languages with non-Latin features. Optimal MMSE and OCS subtest cut-offs were similar across WEIRD and less WEIRD populations, whereas optimal MoCA cut-offs appeared lower for less WEIRD populations. The use of adjusted scores resulted in different optimal cut-offs or similar cut-offs with better accuracy.

Conclusions: MoCA, MMSE and OCS, are promising tools for diagnosing post-stroke-NCD. For culturally diverse populations, translation, adaptation and adjusted scores or cut-offs are necessary for diagnostic accuracy. Available studies report scarcely about their sample's cultural background and there is a lack of diagnostic accuracy studies in less WEIRD or culturally diverse populations. Future studies should report more cultural characteristics of their sample to provide better insight into the tests' accuracy in culturally diverse populations.

Keywords: cerebrovascular disease, post-stroke cognitive impairment, cognitive screening test,

diagnostic test accuracy, cultural diversity, population appropriate normative data

Introduction

Worldwide, stroke is a leading cause of death and disability (Feigin et al., 2021; Kim et al., 2020). The burden, indicated by the annual number of strokes, deaths and years lost due to disability, has increased in the past decades and is extensively larger for low income and lower-middle income countries. Neurocognitive disorders (NCD) are common post-stroke. Research presented NCD prevalence rates varying from 18% to 82% and a pooled prevalence of 38% within the first year post-stroke (Sexton et al., 2019; Sun et al., 2014). Even after successful clinical recovery post-stroke NCDs persist and are strongly associated with disability and functional dependence (Jokinen et al., 2015; Lawrence et al., 2001; Nys et al., 2007). Early and efficient assessment of NCD post-stroke is therefore important.

Cognitive screening post-stroke

Different tests and criteria are used across studies to diagnose NCDs post-stroke (Sexton et al., 2019; Sun et al., 2014). The DSM-5 does not specify which tests should be used, but does advise the use of tests where performance is compared to normative data appropriate for the patient's age, educational attainment and cultural-linguistic background. Brief screening tools are recommended if formal neuropsychological testing is not available or feasible (Quinn et al., 2018; Sachdev et al., 2014). The Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005) and Mini-Mental State Examination (MMSE, Folstein et al., 1975), which were developed for detection of Alzheimer's dementia and mild cognitive impairment, are the most commonly used screening tools for post-stroke NCD. Systematic reviews have concluded that MMSE is accurate for detecting major NCD post-stroke (i.e., dementia), while MoCA is accurate for detecting post-stroke NCD in general (Burton & Tyson, 2015; Koski, 2013; Shi et al., 2018). However, the MMSE is inaccurate for detection of executive dysfunction, and neither MMSE nor MoCA assess common post-stroke cognitive impairments such as visual neglect, apraxia and reading and writing deficits (Kosgallana et al., 2019; Stolwyk et al., 2014; Van Heugten et al., 2015). Furthermore, both MMSE and MoCA are domain-general screening tools (i.e., tools that result in one score for general cognitive performance) with tasks that require intact visual and verbal abilities. As visual neglect, aphasia and reading and writing deficits are common post-stroke, these might confound performance on the MMSE and MoCA (Demeyere et al., 2015). Consequently, the Oxford Cognitive Screen (OCS, Demeyere et al., 2015) was developed for post-stroke NCD. It is a domain-specific tool that is more inclusive for patients with aphasia and neglect, and less confounded by co-occurring cognitive difficulties.

Cultural diversity and cognitive screening

Although the MMSE, MoCA and OCS are promising tools for post-stroke NCD, these tests have been developed in a certain cultural population. The cultural background of populations can be characterized as western, educated, industrialized, rich and democratic (WEIRD) or less WEIRD

(Henrich et al., 2010). Populations can also be described using other cultural factors such as ethnicity, languages, worldview or religions and country of birth, where more variety in cultural factors indicates higher cultural diversity (Gören, 2013; Moieni et al., 2017). As these factors are not mentioned in the original studies of the MMSE, MoCA, and OCS, it is difficult to accurately describe the cultural background and diversity of the populations in which these tests were developed and normed. The MMSE, MoCA and OCS have been developed in the United States of America, Canada and the United Kingdom, respectively. These countries are classified as countries with WEIRD populations (Henrich et al., 2010; Klein et al., 2018).

Different sources of bias, i.e., construct bias, method bias, item bias, can cause cognitive screening tools to be less accurate in measuring the real underlying cognitive in different cultural populations (e.g., less WEIRD populations; Fernández & Abe, 2018; van de Vijver & Tanzer, 2004). Construct bias occurs when the cognitive function that is measured is not equivalent across cultural populations or when the same tests measure different cognitive functions across populations. Method bias occurs when methodological issues cause differences in performance between populations. It occurs, for example, when (1) the background (e.g., age, education, selection criteria) of the population in which the tool will be used, is incomparable to the population in which the tool was developed and normed, (2) the content of the tools or the methods of testing are less familiar for the population in which the tool will be used, or (3) language or communication differences influence performance. Item bias occurs when people with the same underlying cognitive ability from different populations perform differently on test items, because items have different meanings across these populations. Examples for tests that are vulnerable to these sources of bias are trail making, figure copy, naming and calculation and number processing tests (Fernández & Abe, 2018), tests that are often included in screening tests such as the MMSE, MoCA and OCS.

Cultural adaptation and norming of tests

When bias is suspected, cultural adaptation and norming of tests is a preferred and effective approach to ensure construct validity (Fernández & Abe, 2018); adapting and norming tests (or test items) ensures that the tests (and the test items) measure the cognitive functions it was supposed to measure in the culturally different population. Fortunately, the MMSE, MoCA and OCS have been translated or adapted for several cultural populations; mostly for populations residing in one city or country speaking one similar language. Currently, there are 75 translated MMSE versions (https://www.parinc.com/products/pkey/237), 74 translated and adapted MoCA versions (www.mocatest.org) and eight translated and adapted OCS versions (www.ocs-test.org), and other translations and adaptations are underway. Previous research has shown that age and education adjusted cut-offs are necessary for accurately diagnosing cognitive impairment or (Alzheimer's) dementia with the MMSE (e.g., Escobar et al., 1986; Han et al., 2008; Kochhann et al., 2009) and MoCA (e.g., Borland et al., 2017; Din et al., 2016; Kessels et al., 2022; Rossetti et al., 2011). Previous research has also shown that optimal cut-offs for diagnosing dementia differ even when populations have similar educational levels or when test scores are corrected for age and education. For example, differences were found for the MMSE between an urban and rural sample in Brazil (Pedraza et al., 2012), between two different ethnic populations in the United States of America (Brucki & Nitrini, 2010), and between three different ethnic samples in Singapore (Ng et al., 2007). Similarly, different optimal MoCA cut-offs were also found for different ethnic-racial samples with same educational levels in the United States of America (Milani et al., 2018). It is therefore necessary to compare the optimal cut-offs and diagnostic accuracy of the MMSE, MoCA and OCS for detecting post-stroke NCD between culturally different populations. Differences in diagnostic accuracy and optimal cut-offs can indicate a bias in diagnosing post-stroke NCD with the MMSE, MoCA or OCS in culturally diverse populations (e.g., less WEIRD populations). As worldwide migration trends show an increasing cultural diversity within countries' populations (United Nations, 2002, 2009), this might be even more relevant.

The aim of this systematic review therefore is to review the appropriateness of the MMSE, MoCA and OCS for measuring post-stroke neurocognitive disorders in culturally diverse populations, including, but not limited to less WEIRD populations. Objectives are to compare translations and/or adaptations, adjustments in scores, optimal cut-offs, and diagnostic accuracy of different versions *across* stroke populations with different cultural backgrounds and synthesize this information to assess the appropriateness of the MMSE, MoCA and OCS for diagnosing neurocognitive disorders *in* culturally diverse stroke populations.

Methods

Search strategy

The systematic literature search was independently conducted by two reviewers in the databases PubMed (MEDLINE), EMBASE, CINAHL and Web of Science Core collection, from the earliest available dates stated in the individual databases until September, 30th 2021. The search string included synonyms for stroke, synonyms for cognitive impairment, the three tools MoCA, MMSE and OCS, and several terms for psychometric properties and was adapted to each database (see Supplemental table 1).

Eligibility criteria

Studies were eligible for inclusion if they met the following criteria: (1) the participants were adults (18 years or older) with cerebrovascular accident, as diagnosed by brain scan or with clinical judgement, (2) the studied topic was neurocognitive disorders post-stroke , (3) the tests of interest were Montreal Cognitive Impairment (MoCA), Mini-Mental State Examination (MMSE) or Oxford Cognitive Screen (OCS), (4) the outcomes were diagnostic test accuracy (DTA) statistics of one of these three screening tools, and (5) full-text was available in English. Systematic reviews were excluded.

Data selection and extraction method

After removal of duplicates, titles and abstracts were screened for the inclusion criteria. Full texts of potentially eligible articles were then retrieved and assessed for inclusion. To increase the reliability of the results, this selection and extraction process was conducted independently by two reviewers. Disagreements between the reviewers were dissolved by discussion with a supervisor. Reasons for exclusion were recorded. A standardized extraction sheet was used to extract the following data: study information (e.g., authors, year of publication, country of origin, type of study), samples' information (e.g. number of participants, mean and standard deviation of age, education, type of stroke, participant selection/exclusion criteria), screening test information (e.g., version of screening tool used and adaptation information), reference standard information (e.g., used method and criteria for diagnosing post-stroke NCD), testing time post-stroke, cut-offs and diagnostic test accuracy data. If (part of the) data from studies was mentioned in other cited articles, it was extracted from those cited articles. This happened regularly because information about the version and adaptation of the screening tools was usually described in other articles.

Data analysis and synthesis method

A qualitative synthesis was conducted. First, study characteristics such as study methods, sample characteristics and cultural diversity of all included DTA studies were explored. Study methods were explored by summarizing used study designs, reference standards and time of testing post-stroke. Sample characteristics were explored by summarizing most frequently used inclusion and exclusion criteria. The sociodemographic and cultural diversity of the studies was explored. Due to the lack of information about each study sample's cultural background, studies could only be grouped based on how Western, Educated, Industrialized, Rich and Democratic (WEIRD) the countries of the studies were (Henrich et al., 2010; Klein et al., 2018). Using this five-dimension method, Klein et al. (2018) calculated a WEIRDness score and divided countries into two groups WEIRD (score of .70 or higher) or less WEIRD. For countries not yet in their list, a WEIRDness score was calculated using the same method.

Second, MMSE, MoCA and OCS studies in the stroke population were synthesized separately. Different versions, their adaptations and their optimal cut-offs were compared. Optimal cut-offs were selected using highest Youden Index (Böhning et al., 2008; Youden, 1950). The Youden Index (YI) is a measure that integrates a tests' diagnostic accuracy statistics (i.e., YI = sensitivity + specificity – 1) into one score ranging from 0 to 1 with 1 indicating perfect test accuracy (i.e., no false positives and no false negatives) and 0 indicating no diagnostic value. As there was no empirical literature on what value of the Youden Index (YI) is satisfactory for diagnostic accuracy, cut-offs with a YI ≥ .50 were deemed satisfactory for this review. A YI at or higher than .50 assures that the tests' integrated sensitivity and specificity are at least midway towards perfect accuracy (Power et al., 2013). Information about the use of adjusted scores, and their influence on the cut-offs and diagnostic accuracy statistics such as YI and area under the curve (AUC), were synthesized. Optimal cut-offs and their YI were synthesized for minor NCD, major NCD or NCD in general for WEIRD and less WEIRD populations. Minor NCD, major NCD and NCD in general were defined as (1) a performance of at least 1 standard deviation below norms on at least one cognitive test, without impairment in daily functioning, (2) a performance of at least 2 standard deviations below norms or/and impairment in daily functioning, and (3) a performance of at least 1 standard deviation below norms without further categorization into minor or major, respectively (American Psychiatric Association, 2013). The qualitative review was not followed by a meta-analysis, because results from the meta-analysis might not be reliable due to the heterogeneity in (unreported and reported) sample characteristics and study methodology between the studies (Khaw et al., 2021; Lijmer et al., 1999; Whiting et al., 2013). A summary of the found heterogeneity is included in the results.

Results

Study selection

The systematic search resulted in 1796 records, for which 787 duplicates were removed. Researchers suggested three more records. The abstracts from 1012 records were examined for inclusion. Finally, 54 studies were included after full-text review. The process and outcome of the systematic search is presented in a flowchart in figure 1.

The sociodemographic and cultural diversity of retrieved studies

The DTA studies (N=54) were done in 17 countries. Thirty-three DTA studies were done in 13 WEIRD countries in Europe (N=26), North America (N=5) and Australia (N=2). The other 21 DTA studies were done in four less WEIRD countries in Asia (i.e., China (N=15), Singapore (N=4) and Russia (N=1)) and South America (i.e., Peru). There were no studies for Africa. Most studies (N=51) reported some information on the age of their participants. Most of those studies had participants with an average age above 60 years; there were five studies with an average age lower than 50 years and no studies with an average age below 40 years. Many studies (N=41) reported some information on the education of their participants. 27 studies reported the average years of education and the lowest average was 8.7 years for studies in WEIRD countries and 7.5 years for studies in less WEIRD countries. The 14 other studies mostly reported percentages for which 10 studies had participants with primary or lower education with percentages ranging between 12 and 75. Nine studies excluded illiterates. One study reported socio-economic status. The language of testing, although not explicitly written in many studies, could be identified for 33 studies and those languages were English (N=12), Chinese or Chinese dialect (N=11), Dutch (N=4), Italian (N=3), Spanish (N=2), French (N=1), Bulgarian (N=1), Slovenian (N=1) and Russian (N=1). 21 studies required participants to be a native or fluent speaker of the language of testing. The nationality or ethnicity of participants was briefly reported (i.e., “Italian”, “Norwegian”, “Spanish”, “White”, “Russian”, “Chinese”) by 19 studies, for which 14 were Asian studies with Chinese participants. One study reported that participants lived outside the urban city.

Mini-Mental State Examination

Translated or adapted versions

Twelve out of 75 MMSE versions have been analyzed for accuracy for diagnosing NCD in the stroke population. These versions and their reported cut-offs are presented in Table 1. Little to no information about the translation or adaptation was mentioned in the studies. The original MMSE article (Folstein et al., 1975) was often cited instead of the source of the adapted version. MMSE versions were mostly translations and sometimes adaptations in the attention task (i.e., a different word for backward spelling), the memory task (i.e., different words or objects) and the language task (i.e., a different sentence). 16 out of 28 studies were done in WEIRD countries, i.e., English version in United Kingdom (Blake et al., 2002; Brookes et al., 2015; Pendlebury et al., 2012, 2013), Sweden (Agrell & Dehlin, 2000), Norway (Fure et al., 2006), Australia (Cumming et al., 2013; Srikanth et al., 2006) and United States of America (Grace et al., 1995), Dutch version in The Netherlands (Bour et al., 2010; Nys et al., 2005) and a version in France (Godefroy et al., 2011). The other studies (N=12) were done in three less WEIRD countries, i.e., China, Singapore and Peru using the Chinese (Shen et al., 2016; Xu et al., 2014; Xu et al., 2021; Zhang et al., 2016; Zhu et al., 2020) and Cantonese (G. K. C. Wong et al., 2012), the Singaporean Chinese, Malay and English (Dong et al., 2014; Dong et al., 2012), and the Peruvian Spanish (Custodio et al., 2021) versions, respectively. There were no studies for Africa, and no studies for the many other countries in Asia and South America.

Diagnostic Test Accuracy

The systematic search resulted in 28 DTA studies. Reported optimal cut-offs for diagnosing NCD post-stroke vary from 23 to 30, with an overall trend of almost similar cutoffs for less WEIRD and WEIRD populations (Table 1). Overall, the YI was slightly below .50 for both populations, and only ≥ .50 for diagnosis of Major NCD in less WEIRD populations (Table 2). The DTA studies differed a lot in studied stroke population (e.g., stroke type, testing time post-stroke) and reference standard (e.g., used tests and criteria, testing time post-stroke), making comparison of the cut-offs and accuracy statistics between versions difficult. Detailed data from these studies can be found in Supplemental tables 2 and 3. One study found that the English MMSE was not accurate for right-hemispheric stroke (Grace et al., 1995) and argued that this might be explained by the fact that only one item from the MMSE – the construction item – is related to right-hemispheric lesion. Another study, however, found no differences in accuracy between left- and right-hemispheric stroke patients (Cumming et al., 2013). One study also found that the MMSE was not accurate for patients with only memory impairment (Blake et al., 2002) and another study found that the maximum score 30 was the optimal cut-off for single domain mild cognitive impairment (Pendlebury et al., 2013). No clear accuracy trend for specific stroke types could be noticed, but studies that included only lacunar stroke patients always had accuracy statistics with a YI below .50. More stringent criteria for NCD often resulted in lower optimal cut-offs. When NCD was defined as 1 or 1.5 standard deviations below the mean, optimal cut-offs were often the same, but when it was defined as 2 standard deviations below the mean, optimal cut-offs were often one point lower (Chen et al., 2020; Cumming et al., 2013; Pendlebury et al., 2013). Similarly, when NCD was defined as deviant performance on more tests or more domains, optimal cut-offs were usually one point lower (Bour et al., 2010; Pendlebury et al., 2013; Xu et al., 2021).

Population-adjusted scores or cut-offs

Few studies mentioned score adjustment for gender, age and/or education. There were no studies adjusting for other factors such as cultural characteristics. Five studies analyzed the diagnostic test accuracy using gender, age and/or education adjustment. For the Chinese and Singaporean MMSE the use of adjustment resulted in better area under the curve (AUC, Dong et al., 2012; Dong et al., 2014; Xu et al., 2014; Zhu et al., 2020). For the French MMSE it resulted in a slightly lower AUC, but the Youden index was higher (Godefroy et al., 2011). The Chinese and Singaporean studies adjusted the scores using regression, but the MMSE score adjustment (e.g., points added or subtracted) for gender, age and/or education is not clearly mentioned. For the Chinese study, the optimal score after adjustment for age and education was the same for diagnosis of minor NCD (i.e., 29), but was one point lower (i.e., from 27 to 26) for distinction between minor and major NCD (Xu et al., 2014). The Singaporean studies did not report optimal cut-offs for adjusted scores. For the French version one point was added for patients with primary education or less (≤8 education years) and one point was subtracted for patients with tertiary education (≥12 education years), but the optimal cut-off was the same before and after adjustment for education. One Chinese DTA study mentioned different cut-offs for educational levels, i.e., a cut-off of 17 for illiteracy, 20 for primary school and 24 for middle school or higher, but ultimately reported one cut-off of 29 which had a unsatisfactory YI of 0.21 (Zhao et al., 2012).

Montreal Cognitive Assessment

Translated or adapted versions

Ten studies, i.e., studies from France, Italy, Sweden, Norway, China and Singapore, did not report the version (Abzhandadze et al., 2018, 2019; Y. H. Dong et al., 2012; Godefroy et al., 2011; Munthe-Kaas et al., 2021; Wu et al., 2013). Other studies mentioned the version, but cited the original MoCA source (i.e., Nasreddine et al., 2005). Little information was reported about the translations or adaptations. Through comparison of the versions from the official MoCA website information about the adaptations was retrieved. Most studies used versions with adaptations in the tasks trail making, visuoperception, naming, attention, sentence repetition and verbal fluency (Table 3). Adaptations were more often done for less WEIRD countries (e.g., China and Singapore) and countries with a non-roman alphabet (e.g., China, Singapore, Bulgaria). To improve the content for lower educated populations the trail making test and the cube and clock tests were changed into somewhat different tests, i.e., a trail making test without the alphabet and a visuoperception test with naming of overlapping objects, respectively. Beside culturally adapted versions, shorter MoCA versions were also studied. The 5-minute National Institute for Neurological Disorders and Stroke-Canadian Stroke Network (5-min NINDS-CSN) version was the most studied short MoCA version (Bocti et al., 2013; Dong et al., 2016; Feng et al., 2021; Wei et al., 2020). This version consists of three MoCA items, i.e., orientation, delayed recall and verbal fluency, resulting in a total score of 12, instead of the original 30. Another short version was the Bocti short form MoCA, which consists of five MoCA items, i.e., verbal fluency, cube copy, trail making, delayed recall and abstraction, resulting in a total score of 10 (Bocti et al., 2013; Campbell et al., 2015; Wei et al., 2020). A last, less studied short version was a 5-minute protocol with three MoCA items, i.e., delayed recall with maximum 5 points, verbal fluency, and cued recall, with a total score of 30 points (Feng et al., 2021). Similar to the MMSE DTA studies, most MoCA DTA studies were also done in WEIRD countries. All studies in less WEIRD countries were from China or Singapore. There were no DTA studies for South America, Africa and other Asian countries.

Diagnostic Test Accuracy

The systematic search resulted in 37 DTA studies with the MoCA. Reported optimal cut-offs for diagnosing post-stroke NCD varied from 16 to 27, with lower cut-offs for less WEIRD studies compared to WEIRD studies (Table 4). Overall, the YI was ≥.50 in both WEIRD and less WEIRD studies (Table 5). Similar to the MMSE studies, the methodology between MoCA DTA studies also differed al lot, making comparison of cut-offs and accuracy statistics difficult. Detailed data from these studies can be found in Supplemental tables 2 and 4. One study found that the English MoCA had poorer accuracy for right-hemispheric stroke patients and argued that right-hemispheric stroke patients have impairments in intellectual functioning, information processing speed, and non-verbal memory, and that these cognitive functions are not measured by the MoCA (Chan et al., 2017). Another study, however, found higher accuracy for right-hemispheric stroke (Cumming et al., 2013) and argued that this was because MoCA measures attentional and visuospatial deficits which are typical for right-hemispheric stroke. Accuracy was unsatisfactory for the Basic MoCA version and for some shorter MoCA versions. As noticed before with the MMSE studies, MoCA studies with more stringent criteria for the reference standard also resulted in lower optimal cut-offs (Chen et al., 2020; Jaywant et al., 2017; Pendlebury et al., 2013). Two Canadian studies suggested a different, three category approach using maximum sensitivity and specificity (>.90) for better accuracy (Swartz et al., 2016; Zaidi et al., 2020). Based on this method low, intermediate or high probability for NCD is determined using the upper cut-off with maximum sensitivity and the lower cut-off with maximum specificity. For both studies the upper cut-off was the same (i.e., 27), while the lower cut-off was higher for the study with less stringent criteria for the reference standard (i.e., 24 versus 23). This approach has not been validated by other studies yet.

Population-adjusted scores or cut-offs

There were no studies with adjustment for cultural characteristics. Adjustment was often done for gender, age and/or education. Many studies mentioned the use of the original adjustment of +1 point for 12 or less years of education. Chinese MoCA studies with the Changsha and Mandarin versions instead added 1 point for less than 6 years of education (Feng et al., 2021; Tu et al., 2013; Zhu et al., 2020). Arguments for keeping or adapting the original score adjustment are not mentioned. One Chinese study showed that higher educational levels resulted in lower sensitivity and higher specificity for the same cut-off, but a relatively stable YI (Wu et al., 2013). Four studies analyzed the diagnostic test accuracy using regression adjusted scores. The use of gender, age, and education adjusted scores for the Chinese Beijing version resulted in the same optimal cut-off and higher accuracy statistics for diagnosing minor NCD, and a lower optimal cut-off (from 21 to 19) for diagnosing major NCD (Xu et al., 2014). Singaporean studies also found higher AUC for age and education adjusted scores, but did not report an optimal cut-off for adjusted scores (Dong et al., 2012; Dong et al., 2014). In contrast to the Chinese study, the use of age and education adjustment resulted in higher optimal cut-offs (from 20 to 23) for the French study (Godefroy et al., 2011). Two studies, i.e., from Sweden (Abzhandadze et al., 2019) and Portugal (Freitas et al., 2012), mentioned education adjusted scores for non-stroke population, but did not use adjustment for their DTA analysis.

Oxford Cognitive Screen

Translated or adapted versions

Diagnostic test accuracy has been analyzed for the English, Italian, Dutch, Spanish, Putonghua (Mandarin) and Russian OCS (Demeyere et al., 2015; Hong et al., 2018; Huygelier et al., 2022; Mancuso et al., 2018; Shendyapina et al., 2019; Valera-Gran et al., 2018). The validity of the Hong Kong Cantonese version has also been studied in chronic stroke patients, but no accuracy statistics are presented for the cut-offs (Kong et al., 2015). The subtest that needed most adaptation was Sentence Reading, especially for languages with unique features (i.e., Russian, Putonghua) compared to languages with features from the Latin alphabet (e.g., English, Spanish, Italian). Other subtests that needed adaptation were Picture naming, Verbal and Episodic memory. The subtests Picture pointing (Semantics), Visual Field, Gesture imitation (Praxis), Number writing, Calculation, Hearts cancellation and Executive function were mostly non-verbal and only needed translation of instructions.

Diagnostic Test Accuracy

The diagnostic test accuracy studies for the OCS differed from those for the MMSE and MoCA studies. In contrast to the MMSE and MoCA, the OCS resulted in scores for specific cognitive domains. Therefore, a different test was used to analyze the accuracy of each OCS subtest, instead of one reference standard. The five retrieved studies with diagnostic test accuracy statistics for the OCS are presented Table 3. The English, Spanish, Putonghua and Russian studies used equivalent tests, usually subtests from the MoCA, to calculate sensitivity and specificity for OCS subtests. The Italian and Dutch (Flemish) study calculated the sensitivity for impairment in any cognitive domain in comparison to the Italian MMSE (cutoff < 22) and Dutch MoCA (cut-off < 26), respectively. The English and Russian versions calculated accuracy statistics for the 5th percentile cut-offs from a healthy group, while the Spanish and Putonghua versions sought optimal cut-offs using the YI. Cut-off scores from the versions are quite similar. Some differences in cut-offs are observed for subtests with larger score ranges, i.e., subtest for attention, executive and praxis domains. Overall, unsatisfactory (YI <.50) sensitivity and specificity statistics were reported for subtests. Only the

Russian OCS had satisfactory diagnostic accuracy for almost all subtests. The Putonghua OCS also had satisfactory accuracy for subtests, i.e., for the Picture naming score, a combined score for Verbal and episodic recognition, a combined score for Number cognition, and the Gesture imitation score. The English and Spanish OCS also had satisfactory accuracy for Gesture imitation, and for Hearts cancellation. The main difference in methodology between the Russian and other studies was the timing of testing. The Russian version was used at 8 ± 19 months post-stroke, while the other studies screened patients between 0- and 3-months post-stroke.

Population-adjusted scores or cut-offs

The English OCS study reported effects of age and education, especially on the Executive and the Sentence reading subtests, but could not calculate and use adjusted cut-off scores due to a small sample size (Demeyere et al., 2015). The Russian, Spanish and Italian studies also observed age and education effects (Mancuso et al., 2018; Shendyapina et al., 2019; Valera-Gran et al., 2018), but only the Italian study calculated and used adjusted cut-offs. It, however, didn't analyze the accuracy of each OCS subtest. No score adjustment for other factors, e.g., cultural characteristics, was found.

Heterogeneity in study methods of retrieved studies

The included studies differed substantially in study methods, in particular in study design, the reference standard and criteria for diagnosing NCD, time of testing with the screening test and the reference standard, and participants inclusion and exclusion criteria. The study design of most studies was cross-sectional with stroke patients only. Some studies were case-control studies where stroke (minor or major NCD) patients were compared to neurotypical adults without NCD. The reference standard for diagnosing NCD was often a neuropsychological test battery, but sometimes also a screening test (such as MMSE or MoCA) or clinical evaluation by a specialist. In few studies the reference standard was limited to a functional independence measure. Even though a neuropsychological test battery was the most frequent choice, the criteria for NCD differed a lot across studies. The time post-stroke when the screening instrument was administered also differed from 36 hours to 35 years post-stroke. Most of the time the reference standard was administered at the same time of the screening test, but sometimes at 3, 6, 12 months or other time period after screening. The inclusion and exclusion criteria for the stroke sample also differed. Some studies only included a certain type of stroke patients. Almost all studies excluded patients with brain disorders other than stroke, or psychiatric or other medical disorders and problems hindering testing, but the list of excluded disorders or comorbidities differed across studies. Detailed information can be found in Supplemental Tables 3, 4, 5 and 6.

Discussion

Stroke is worldwide leading cause of disability and its burden is larger for lower middle-income countries (Feigin et al., 2021; Kim et al., 2020). NCDs are very common after stroke and persist even when no functional disability is visible (Jokinen et al., 2015). Early assessment is therefore necessary. Several systematic reviews have studied the accuracy of the MoCA and MMSE, and the more recently developed OCS (Burton & Tyson, 2015; Kosgallana et al., 2019; Shi et al., 2018), but it is still unclear how appropriate or accurate the MMSE, MoCA and OCS are for use in culturally diverse populations as reviews often do not describe the versions and backgrounds of the studied populations. To address this issue the current systematic review aimed to assess how appropriate MMSE, MoCA and OCS are for measuring NCD post-stroke in culturally diverse populations, by comparing test versions and used cut-off criteria, as well as the validity and accuracy of these different versions, across culturally different stroke populations.

Population-appropriate content

The MMSE, MoCA and OCS all needed translation and sometimes also cultural adaptation. Across studies simple translations were sufficient if the language shared similar features with English, which was the language of the original test versions. For languages with different, non-Latin alphabet features, the translation process was more complex, and adaptation was necessary. This was the case for MoCA's trail making and sentence repetition and OCS's sentence reading test. For WEIRD populations, translation was sufficient, but cultural adaptation was often needed for less WEIRD populations. Adaptations sometimes were simple, but sometimes more complex. Simple adaptations were usually changes from uncommon pictures and words to more common pictures and words, e.g., for MMSE's memory and sentence repetition, MoCA's naming, memory and sentence reading, and OCS's naming and sentence reading verbal and episodic memory. Complex adaptations were changes in 'the method of testing', e.g., changing MoCA's trail making into a version without letters, changing MoCA's cube copying and clock into naming of overlapping objects, changing MoCA's letter fluency into category fluency. This was often done for lower educated populations and populations with languages without a Latin-like alphabet, because the original method of testing had a higher difficulty or was less familiar to the target population. In summary, without translation and adaptation, (items or tasks from) the MMSE, MoCA and OCS might not be appropriate for detecting post-stroke NCD in culturally diverse populations. When cultural-linguistic differences between populations are larger, complex adaptation should be considered to accurately measure the intended cognitive functions. Khan et al. 2022 developed a useful guideline for translation and adaptation of the MoCA (Khan et al., 2022). Noteworthy, when it is (too) difficult to maintain construct equivalence with adaptation, development of a cross-cultural cognitive screening test for post-stroke NCD, is a better option (Fernández & Abe, 2018).

Diagnostic test accuracy

The optimal cut-offs for the MMSE and MoCA versions varied a lot across populations. The optimal MMSE cut-offs were similar in less WEIRD and WEIRD populations, whereas the optimal MoCA cut-offs seemed to be lower in less WEIRD populations. Overall, the accuracy of the MMSE was slightly below satisfactory threshold (i.e., YI < .50), whereas the accuracy of the MoCA was at or slightly above this threshold (i.e., ≥ .50), for WEIRD and less WEIRD populations. Unsatisfactory MMSE accuracy was noticed for patients with lacunar stroke, right-sided stroke or only memory or single domain impairment. Unsatisfactory MoCA accuracy was noticed for the MoCA Basic version and some shorter versions. So far, accuracy has been studied less frequently for the more recently developed OCS. The optimal cut-offs for the OCS subtests were quite similar across the few studied populations. Differences in optimal cut-offs were mostly noticed for OCS subtests with larger score ranges, i.e., Hearts cancellation, Gesture imitation and Executive task. Only the Russian OCS had satisfactory accuracy for all subtests. The subtests Gesture Imitation and Hearts cancellation often had satisfactory accuracy, and these are the subtest with the largest score ranges. The Putonghua version added subtests for memory and numeric cognition together, which resulted in larger score ranges, and better accuracy. More diagnostic test accuracy studies are needed for the OCS. In summary, without adaptation of the cut-offs for the target population, adaptations (adapted versions) of the MMSE, MoCA and OCS might still be less accurate or appropriate for detecting post-stroke NCD in culturally diverse populations. Diagnostic test accuracy studies are needed to identify the optimal and accurate cut-off in culturally diverse populations.

Population-adjusted scores or cut-offs

Optimal cut-offs for MMSE and MoCA not only differed across different cultural populations, but also within. Although previous research has shown that gender, age and education might affect MMSE, MoCA and OCS scores (Huygelier et al., 2020; O’Driscoll & Shaikh, 2017; Rossetti et al., 2011; Shim et al., 2017; Steis & Schrauf, 2009), few studies have included these factors in their diagnostic test accuracy analysis. MMSE and MoCA studies that included these factors, have done that by adjusting MMSE or MoCA scores using regression. One study from the OCS conducted the diagnostic test accuracy with gender, age and education adjusted 5th percentile cut-offs from a healthy sample. For MoCA and MMSE studies, optimal cut-offs for adjusted scores were sometimes higher or lower than the optimal cut-off for non-adjusted scores, while some stayed the same, but had better accuracy. These findings are similar to those from a large-scale study with the Hong Kong MoCA which found a large discrepancy in diagnosis when using the original and local-found cut-off versus when using age or education adjusted cut-offs (Wong et al., 2015). These few results suggest that gender, age and education influence accuracy, and that incorporating these factors in tests scoring might improve diagnostic test accuracy for the MMSE and MoCA. In summary, and as advised in the DSM-5, normative data (i.e., cut-offs) appropriate for different age, educational and cultural-linguistic backgrounds should be considered, instead of one cut-off for a country's population. If population-adjusted cut-offs for post-stroke NCD are less achievable via diagnostic test accuracy studies, normative data from the healthy target population can also be very useful.

Limitations

This systematic review has some limitations. A first limitation is that the quality of the analysis is dependent on the retrieved studies. The review is limited to a synthesis, even though more powerful analysis methods, e.g., meta-analysis, could provide better insights. Using current available studies, a meta-analysis comparing cut-offs and diagnostic accuracy is, however, not reliable due the lack of information about each study's cultural diversity and the large heterogeneity in stroke-related characteristics and study methods of the retrieved studies (Lijmer et al., 1999; Whiting et al., 2013). A second limitation is that most of the studies were done in WEIRD countries in Europe, North America and Australia. Asia, Africa and South America have 48, 54 and 12 countries, respectively, but only four countries have studies with the accuracy of the MMSE, MoCA or OCS for their less WEIRD stroke population. Including only studies with a full-text in English, might have biased the selection of studies in a WEIRD direction; however, only 3 out of 1012 search results were excluded because of the absence of a full-text in English. The lack of studies from less WEIRD or non-Chinese Asian, African and South-American countries limits generalizability of conclusions about the appropriateness of the MMSE, MoCA and OCS for diagnosing NCD in culturally diverse stroke populations. A third limitation is that the diversity of the population in the studies was analyzed using geographic location and the WEIRD classification by country of the study. This is, however, an oversimple classification that underestimates the diversity within WEIRD and less WEIRD countries and that lacks other factors of diversity such as beliefs and practices, acculturation and health literacy. A final limitation is that many studies excluded stroke patients based on their medical history and also stroke-related problems (such as aphasia and paresis) that might hinder testing. The studied stroke populations might therefor differ from clinical reality, limiting the generalizability of results and conclusions.

Conclusion

MoCA and OCS, and MMSE to a lesser extent, are promising tools for screening neurocognitive disorders (NCDs) post-stroke. Translation and adaptation are however necessary to maintain and improve diagnostic accuracy, especially for populations that are more culturally diverse, including populations with languages with non-Latin features and populations that are less WEIRD. Even after test adaptation, adaptation of the cut-off might be necessary. Furthermore, adjustment of test scores or cut-offs for influential factors such as gender, age and education within populations should be considered as these might improve accuracy. Future studies should pursue more homogeneity in study methods and report more cultural characteristics of their sample to provide better insight into the accuracy of these tests across and in culturally diverse stroke populations. More research is necessary in less WEIRD populations and in countries in Africa, South-America and Asia.

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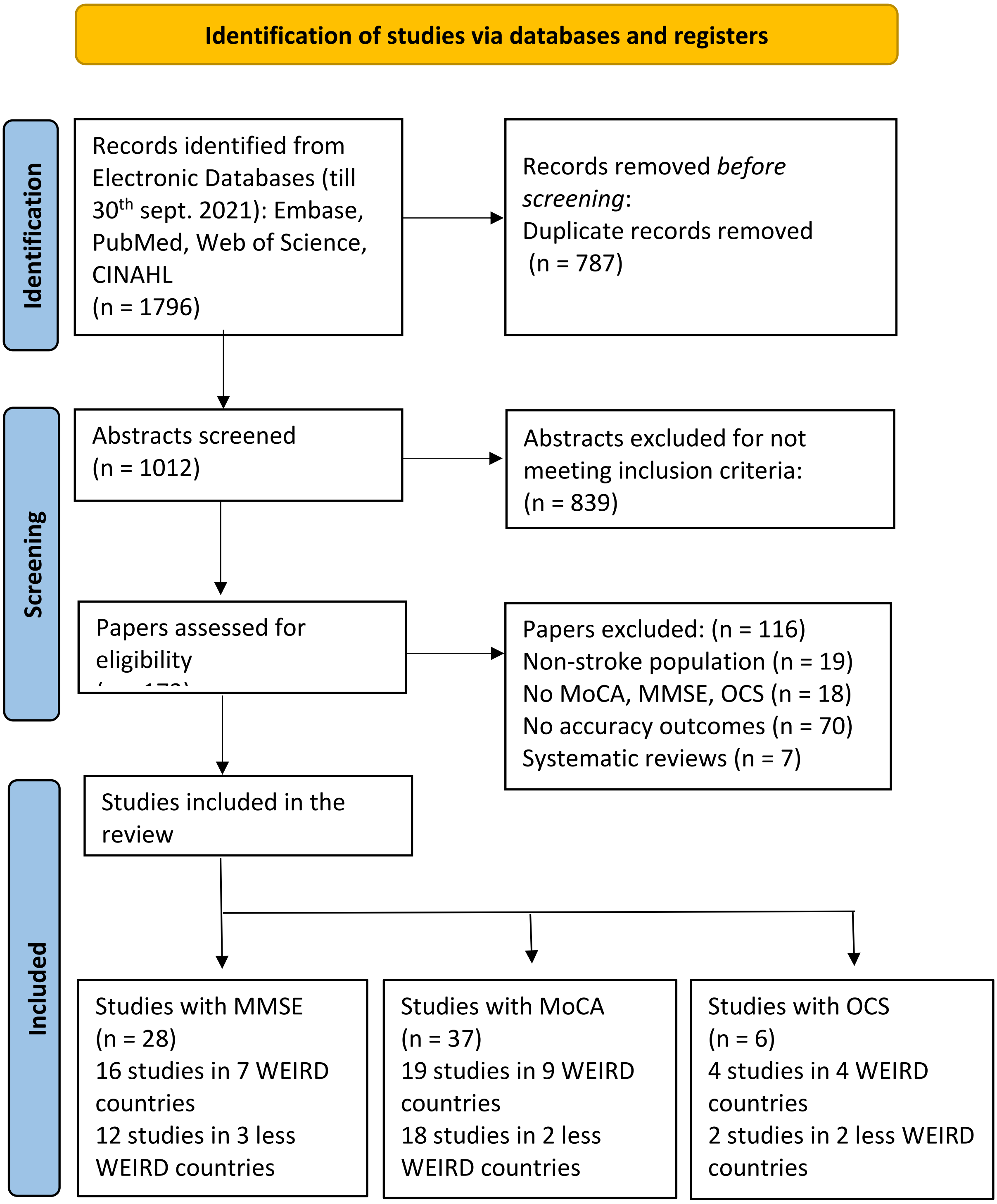
Figure 1

Flowchart for the selection process



Note. MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment; OCS= Oxford Cognitive Screen; WEIRD = western, educated, industrialized, rich and democratic

Table 1

Descriptives for the optimal cut-offs of the Mini-Mental State Examination reported in Western, Educated, Industrialized, Rich and Democratic (WEIRD) versus less WEIRD studies

	WEIRD classification							
	Less WEIRD				WEIRD			
Diagnostic criteria	N	Median	Mean	95% CI	N	Median	Mean	95% CI
Major NCD	11	26.0	25.6	[24.8, 26.4]	9	27.0	26.2	[24.5, 27.9]
Minor NCD	6	27.5	27.7	[26.4, 28.9]	3	29.0	27.3	[20.2, 34.5]
NCD in general	10	27.0	27.1	[26.2, 28.0]	15	27.0	26.9	[26.0, 27.9]
All NCD criteria	27	27.0	26.6	[26.0, 27.2]	27	27.0	26.7	[26.0, 27.5]

Note. NCD = neurocognitive disorders; CI = confidence interval

Table 2

Descriptives for the Youden Index of the optimal cutoffs from the Mini-Mental State Examination reported in Western, Educated, Industrialized, Rich and Democratic (WEIRD) versus less WEIRD studies

	WEIRD classification							
	Less WEIRD				WEIRD			
Diagnostic criteria	N	Median	Mean	95% CI	N	Median	Mean	95% CI
Major NCD	9	0.60	0.56	[0.34, 0.78]	8	0.49	0.48	[0.28, 0.69]
Minor NCD	6	0.41	0.40	[0.21, 0.59]	3	0.46	0.36	[-0.11, 0.82]
NCD in general	9	0.53	0.41	[0.22, 0.59]	15	0.50	0.49	[0.42, 0.57]
All NCD criteria	24	0.54	0.46	[0.36, 0.57]	26	0.49	0.47	[0.40, 0.55]

Note. NCD = neurocognitive disorders; CI = confidence interval

Table 3

Examples of adaptations in the Montreal Cognitive Assessment (MoCA)

MoCA Tasks	Original (English)	Adaptations
Trail making	Switching between numbers and letters	Numbers and Chinese characters or another alphabet; Numbers in white and black; or white and grey; or triangles and circles; or numerals and dices
Visuoperception	Cube copying and Clock drawing	Naming overlapping objects
Naming	Lion, Rhinoceros, Camel or Dromedary	Other more familiar animals such as Duck, Lion, Snake; Elephant instead of Rhinoceros
Memory	Face, Velvet, Church, Daisy, Red	Other more familiar words
Attention	Tapping to letter A	Tapping to a number
Language	Sentence repetition Letter F fluency	Different name in sentence; different sentence Different letter for fluency; or category fluency (e.g., animals)
Orientation	Date, month, year, day, place, city	District (instead of city)
Total score	Add 1 point for 12 or less years of education	Add 1 point for 6 or less years of education (instead of 12 years); or add 1 point for 9 or less years education and subtract 1 point for 12 or more years of education and add 1 point for 75 years age or older and subtract 1 point for 45 years or younger

Table 4

Descriptives for the optimal cut-offs of the Montreal Cognitive Assessment reported in Western, Educated, Industrialized, Rich and Democratic (WEIRD) versus less WEIRD studies

	WEIRD classification							
	Less WEIRD				WEIRD			
Diagnostic criteria	N	Median	Mean	95% CI	N	Median	Mean	95% CI
Major NCD	10	19.0	19.1	[18.1, 20.0]	8	24.5	24.4	[23.5, 27.8]
Minor NCD	10	23.5	24.0	[23.0, 25.0]	4	26.0	26.0	[24.2, 27.8]
NCD in general	18	22.0	22.2	[20.9, 23.5]	23	23.5	24.5	[23.7, 25.2]
All NCD criteria	38	22.0	21.8	[21.0, 22.7]	35	25.0	24.6	[24.1, 25.2]

Note. NCD = neurocognitive disorders; CI = confidence interval

Table 5

Descriptives for the Youden Index of the optimal cutoffs from the Montreal Cognitive Assessment reported in Western, Educated, Industrialized, Rich and Democratic (WEIRD) versus less WEIRD studies

	WEIRD classification							
	Less WEIRD				WEIRD			
Diagnostic criteria	N	Median	Mean	95% CI	N	Median	Mean	95% CI
Major NCD	8	0.60	0.45	[0.16, 0.73]	10	0.50	0.47	[0.34, 0.60]
Minor NCD	10	0.49	0.43	[0.24, 0.62]	4	0.48	0.49	[0.38, 0.60]
NCD in general	22	0.64	0.61	[0.54, 0.68]	30	0.49	0.50	[0.44, 0.57]
All NCD criteria	40	0.58	0.53	[0.46, 0.61]	44	0.49	0.50	[0.45, 0.54]

Note. NCD = neurocognitive disorders; CI = confidence interval

Table 6

Cut-offs and accuracy statistics from the Oxford Cognitive Screen for diagnosing neurocognitive disorder post-stroke

	Oxford Cognitive Screen	**United Kingdom English[a]**			**Spain Spanish[b]**			**Italy Italian[c]**		**Belgium Dutch[d]**		**China Putonghua[b]**	
Domain	Subtest	Cut-off	Se	Sp	Cut-off	Se	Sp	Cut-off	Se	Cut-off	Se	Cut-off	Se
Language	Picture naming	3	0.59	0.73	2	0.32	0.98	2.9-3.7		2-3		3*	0.79
	Semantics	3	0.28	0.98	2	0.15	1.00	3		3			
	Sentence reading	14	0.63	0.82	14	0.54	0.89	14.1-15		14-15			
Memory	Orientation free	4*	0.68	0.87	3	0.52	0.98	3.9-4.0		4			
	Orientation choice				3	0.32	1.00						
	Verbal memory recall				0	0.50	0.96						
	Verbal memory recognition	3	0.75	0.74	3	0.70	0.67	2.4-3.4		2-3			
	Episodic recognition	3			3	0.69	0.78	3.4-3.8		3-4			
	Total recognition											7*	0.71
Attention	Hearts cancellation	42*	0.53	0.70	43*	0.83	0.83	43.4-47.4		37-45			
	Space asymmetry Right / left neglect	-2/2	0.66	0.75	-4/2	0.20/0.43	0.98/0.91	-3/3		-3 - -2/2-3			

	Object asymmetry Right / Left neglect	0/1	0.47	0.91	-1/1	0.15/0.33	0.98/0.98	-2/2		-1-0/0-1			
<u>Numeric</u>	Number writing	3	0.53	0.70	2*	0.61	0.96	2.8-3.0		2-3			
	Calculation	3	0.46	0.91	3	0.52	0.85	3.3-3.8		3-4			
	Total score											6*	0.59
<u>Executive</u>	Executive mixed trails	7						10.5-11					
	Executive score	4	0.67	0.74	0	0.76	0.70	3		-2 - -1			
<u>Praxis</u>	Gestural imitation right/left hand	8*	0.72	0.91	9*/8*	0.72/0.72	0.91/0.94	9		7-11		10*	0.71
Impairment in at least 1 cognitive domain									1.00		0.92, 0.88, 0.68		

Table note. Se = Sensitivity, Sp = Specificity.

[a] Cut-offs are 5th (/95th) percentiles from healthy control group.

[b] Cut-offs are optimal cut-offs using maximal Youden Index.

[c] Cut-offs are 5th (/95th) percentiles from healthy control group adjusted for gender, age or education. Sensitivity in comparison to MMSE<22.

[d] Cut-offs are 5th (/95th) percentiles from healthy group adjusted for age. Sensitivity in comparison to MoCA<26 for <60 years, 60-69 years and 70-91 years, respectively.

* Cut-offs with acceptable Youden Index >.50