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ΒΙΒΛΙΟΓΡΑΦΙΚΗ ΑΝΑΣΚΟΠΗΣΗ | REVIEW PAPER

Limitations and recommendations regarding the Mini-Mental State Examination (MMSE) in illiterate and low educated older adults

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ABSTRACT

Increasing life expectancy has been associated with higher rates of dementia. As illiterate/uneducated individuals are typically over-represented among older cohorts, it is imperative that we identify and/or develop appropriate, non-biased scales and psychometric tests for early detection of, and screening for, cognitive impairment in this group. Given that many traditional neuropsychological tests may underestimate cognitive abilities in illiterate/uneducated and low educated individuals, their use in these groups needs to be reappraised or their format adapted. One of the most commonly used screening tests worldwide is the Mini-Mental State Examination (MMSE). Level of education has been shown to be a significant predictor of performance on the MMSE, hence, there is dispute among researchers related to its applicability in populations with low or no schooling. A wide range of recommendations have been made by scholars for overcoming the education effect on the MMSE, as well as other sources of bias, but some methodological limitations remain, and new ones have emerged concerning its administration to illiterate/uneducated and low educated older individuals. In the present study, we present a theoretical discussion of the challenges inherent in the administration and interpretation of MMSE performance in illiterate/uneducated and low educated individuals, consider previous recommendations and address their limitations, and highlight the optimal methods for clinical assessment of these groups when the MMSE is used.

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Introduction

Early detection and screening for cognitive impairment have become imperative since increasing life expectancy has led to higher rates of dementia than in the past. This increase in dementia prevalence has also been observed among illiterate/uneducated individuals, who are over-represented in older cohorts, especially in low- or middle-income countries (Bertola et al., 2023; Goudsmit et al., 2021). The use of valid measures to improve diagnostic accuracy, particularly in illiterate/uneducated or poorly educated populations, is a great challenge considering that most traditional neuropsychological tests include literacy- or school-dependent items (Aslam et al., 2016; Maher & Calia, 2021; Velayudhan et al., 2014).

Numerous studies have reported the influence of education *per se* as well as the level of education on neuropsychological performance of cognitively healthy illiterate/uneducated individuals, as well as those who are literate but with limited or even more extensive schooling (for a review see Ardila et al., 2010; Mandyla et al., 2021). In fact, several studies have found that healthy individuals with no or limited formal education often performed at a level that is equivalent to that of educated individuals with cognitive decline (Kim & Chey, 2010; Nielsen & Jørgensen, 2013; Youn et al., 2011) or even fail on cognitive tasks altogether (Nitrini et al., 2005). These findings suggest that even in the absence of indications of pathology, and after excluding reading and writing items, older illiterate/uneducated individuals may have difficulty responding accurately on neuropsychological

tests, as performance is affected by educational level and typically requires skills that are mostly obtained in school (Ardila et al., 2010). Inferentially, considering that diagnostic decisions are largely based on deviance from normative data for the individual's peer group, the inability to differentiate healthy individuals from individuals with a progressive neurodegenerative disease increases the odds of misdiagnosis in illiterate/uneducated and low educated populations. Thus, the performance of illiterate/uneducated older adults on current traditional tests may potentially be a misleading criterion for diagnosing dementia (Mandyla et al., 2021).

Among the various cognitive measures available, one of the most commonly used tests worldwide for detecting cognitive impairment is the Mini-Mental State Examination (MMSE) (Folstein et al., 1975). The MMSE is a 30 point-scale (scores range from 0 to 30) assessing orientation, encoding, attention and calculation, recall, language (repetition and complex command), reading, writing, comprehension, and drawing. The most frequently reported cut-points to determine impairment are 23/24 and 24/25 out of a maximum of 30 (Creavin et al., 2016; Lin et al., 2013). The test has been translated into more than 50 languages, has been adjusted for various conditions (e.g., blind patients) (Carnero-Pardo, 2014) and is probably one of the most cited papers in health science (Nilsson, 2007). Given the rates of dementia and illiteracy, as well as the popularity of the MMSE as a screening test for cognitive impairment, the need to explore its efficiency in order to develop a fair neuropsychological assessment for older individuals with no or a few years of education is apparent (Prince et al., 2012; UNESCO, 2018).

Benefits and limitations

The MMSE is one of the most broadly applied brief screening tests for cognitive decline since it has many strengths. The main advantages are that it is a quick, user-friendly instrument (can be administered and evaluated even by non-qualified personnel), there is extensive empirical evidence that supports it, it assesses several cognitive domains, and is useful for follow-up and estimating response to treatment, permitting comparison of results among studies (Carnero-Pardo, 2014; Nieuwenhuis-Mark, 2010).

Despite its benefits, the MMSE presents some structural and psychometric disadvantages, as well as other limitations. Among its basic weaknesses are its limited ability to detect mild cognitive impairment, the lack of standardization, as well as that it was not specifically created to screen for dementia and that it does not measure executive function (for a review see Carnero-Pardo, 2014). Another serious limitation is that the test is affected by socio-demographic variables such as age and education (Monroe & Carter, 2012; Spencer et al., 2013). Because of this, several studies have explored the utility of the MMSE as a dementia screening test in older illiterate/uneducated and low-educated individuals.

The MMSE as a dementia screening test in illiterate/uneducated and low-educated individuals

Concerning the MMSE as a screening test for cognitive decline, the effect of education on performance is one of the most debatable issues throughout the literature. Education is considered an important predictor of MMSE scores and explains a greater part of the variance than do other demographic variables (Bird et al., 1987; Bogiatzidou, 2020; Brayne & Calloway, 1990; Escobar et al., 1986; Fillenbaum et al., 1988; Folstein et al., 1985; Magaziner et al., 1987; Murden et al., 1991; O' Connor et al., 1989; Stewart et al., 1991; Uhlmann & Larson, 1991). In fact, a population-based study in a random sample of Colombian urban and rural residents showed that educational level was positively associated with MMSE score, to a greater extent than age or sex (Rosselli et al., 2000). Furthermore, Ng, Niti, Chiam, and Kua (2007) noted that significant ethnic differences in MMSE scores among Chinese, Malay, and Indian individuals persisted among less educated individuals, even after adjusting for differences in sociodemographic, health, and behavioral variables (Ng et al., 2007). Many reports have shown that illiterate/uneducated or low educated individuals systematically have lower scores on the MMSE compared to their peers with a high educational level (Brito-Marques & Cabral-Filho, 2004; Brucki et al., 2003; Kochhann et al., 2009; Laks et al., 2007; Lourenço et al., 2006; Sczufca et al., 2009; Solias et al., 2014; Tsantali et al., 2012). Others have shown that even when comparing unschooled literate to illiterate individuals, the latter performed more poorly on the MMSE (Mokri et al., 2012). This finding indicates that the acquisition of reading and writing skills *per se*, regardless of formal education, enhances the performance on MMSE, therefore, literacy is also an important variable relevant to MMSE scores.

Illiterate/uneducated or low-educated individuals not only underperform compared to their literate peers, but often their performance is similar to that of cognitively impaired individuals. Ostrosky-Solís, López-Arango, and Ardila (2000) found that the uneducated group had similar scores on the MMSE as the literate group with severe dementia, and the performance of low educated individuals (1 to 4 years of schooling) was equivalent to literate individuals with mild dementia (Ostrosky-Solis et al., 2000). Similarly, others have shown that the MMSE score could not distinguish healthy illiterate from literate individuals with AD (Youn et al., 2011). Additionally, healthy non-readers have been found to have scores that were lower than the cut-off score for dementia, whereas readers (≥ 8 y of formal education) scored above the cut-off (Brucki & Nitrini, 2010; Parker & Philp, 2004). The aforementioned studies indicate that the screening cut-off score (typically 24/25) on the MMSE is probably too high for illiterate/uneducated or low educated individuals (Carnero-Pardo, 2014).

Although the MMSE scoring system has been considered a useful screening measure of global cognitive functioning, scholars have found both ceiling and floor effects. Specifically, there is a high false negative rate in highly educated people and a high false positive effect in people who are older and illiterate (Noroozian et al., 2014). Specifically, the MMSE has been shown to lack sensitivity in highly educated, and specificity in poorly educated (less than high school), persons (Anthony et al., 1982; Shiroky et al., 2007). Based on the recommended cut-off point (23/24), sensitivity was only 66% for dementia and 45% for cognitive impairment in highly educated individuals (≥ 16 y), whereas specificity was 0% for dementia among illiterate individuals residing in a Spanish rural area (Escribano-Aparicio et al., 1999; O'Bryant et al., 2008).

Aside from total scores, many studies have also explored each MMSE item separately and/or each MMSE cognitive domain. Findings have shown that the number of years of education and literacy affects performance on copying a design, reading, writing, and verbal command items; while no demographic variables (education, sex, or age) directly explained memory and attention, self-care ability explained 66.9% of the variance in these domains (Shyu & Yip, 2001). Other studies have reported lower performance of illiterate individuals compared to those who are literate on the MMSE on all items, except repetition, recall, naming (Rosselli et al., 2000), and orientation to time (Bertolucci et al., 1994). Also, a Mexican study that used two domains, namely, no-memory (score 0-24; includes orientation, attention, and language) and memory (score 0-6; includes working and delayed memory) showed that participants with more years of education performed better than those with fewer years of schooling on the total MMSE score and the no-memory domain, but there was no difference on the memory domain (Matallana et al., 2011). Furthermore, Crane and colleagues (2006) classified Italian MMSE results into 10-item bundles in order to determine whether there was differential item functioning (DIF) related to education, age, sex, and occupation. They found that in 6 of the 10 MMSE item bundles, there was DIF related to education and in four of these six bundles there was also DIF related to age. Specifically, items that required reading and writing skills were much more difficult for those with less education (three years or fewer vs three years or more schooling) (Crane et al., 2006). The aforementioned findings highlight the impact of education on MMSE scores and raise concerns about its validity in illiterate/uneducated and low educated populations. At the same time, however, these findings highlight the cognitive domains that might be useful indicators for early detection of dementia in these groups.

Effect of socio-demographic variables

Many researchers have explored the effect of education, as much as other socio-demographic factors (i.e., cultural, socio-economic, age, and sex) on MMSE scores (Matallana et al., 2011; Noroozian et al., 2014). It appears that as age increases and education decreases, the MMSE scores present a wider range (Crum et al., 1993). Internationally, findings have shown that the combination of these two variables amplifies their effect on MMSE performance (Heeren et al., 1990). Indeed, increasing age, lower socioeconomic status, and fewer years of education were all found to be associated with lower scores on the MMSE (Brayne & Calloway, 1990).

Concerning the effect of sex on MMSE performance, results are ambiguous both for total scores and for particular items or cognitive domains. In a number of studies, significant differences have been noted between men and women (Han et al., 2008; Herlitz & Kabir, 2006) with heterogeneous educational backgrounds, that in some cases necessitated the development of different normative data (e.g., Korean MMSE, Italian MMSE) (Foderaro et al., 2022; Han et al., 2008; Ishizaki et al., 1998; Lee et al., 2002). Moreover, another study found that illiterate Bangladeshi women performed more poorly than illiterate men on all tasks, except episodic

memory (Herlitz & Kabir, 2006). In contrast, other studies found no effect of sex on the MMSE (Ishizaki et al., 1998; O'Connor et al., 1989). These conflicting findings may reflect different methods or other factors that may have not been taken into consideration, as well as the heterogeneity of populations with different educational and socio-cultural backgrounds.

With respect to socio-cultural variables, there is evidence that language, cultural differences, occupation, and socio-economic status can affect MMSE scores. For example, a study showed that even after controlling for age and education, farmers scored 2.3 points less than white-collar workers on the MMSE (Frisoni et al., 1993). Moreover, another study in Brazilians aged 50 years and above, with the same educational levels but with different cultural backgrounds, showed that not only education but also environmental and other sociocultural characteristics (i.e., previous history of environmental exposure, occupation) may be associated with performance on the MMSE, even among individuals from the same country and with the same language (Brucki & Nitrini, 2010). Other investigators have also reported that the MMSE score is sensitive to both educational level and cultural background (Bertolucci et al., 1994; Bird et al., 1987; Escobar et al., 1986; Tiwari et al., 2009).

MMSE: dissociating healthy illiterate individuals from those with cognitive decline

Despite the aforementioned findings, which show that the use of the MMSE as a sensitive indicator for cognitive impairment creates a major diagnostic problem due to the effect of education, as well as other socio-demographic factors, on performance, some authors have suggested that it is still a useful test for dissociating healthy illiterate individuals from illiterate individuals with dementia. For instance, a Korean study of older women found that, even though the MMSE scores could not distinguish between healthy illiterate (n=25) and literate individuals with AD (n=25), it could distinguish between healthy illiterate and illiterate individuals with AD (n=25) (Youn et al., 2011). Furthermore, other findings suggest that the MMSE could prove a helpful screening tool when combined with other measures. One such investigation noted that the MMSE and the Pfeffer Functional Activities Questionnaire was the most sensitive combination (94.1%), whereas the most specific was the MMSE and the Clock Drawing Test (89%) when screening for dementia (Aprahamian et al., 2011). Additionally, other investigators have proposed that exploring the relationship among MMSE score, demographic characteristics, and self-care ability ratings, could increase diagnostic accuracy by clarifying what aspects of mental status the MMSE is measuring (Shyu & Yip, 2001). These findings suggest that even though many of the formal tests, such as the MMSE, may underestimate the performance of healthy illiterate older adults when they are compared to their literate counterparts, we should not reject them *in toto*, since they can be helpful as sensitive indicators of the early state of cognitive decline in dementia. Even so, in order to overcome education and/or other biased effects, researchers have developed normative data or new forms of the test for illiterate individuals.

MMSE population-based norms

For the purpose of overcoming any bias inherent in the MMSE relative to older illiterate/uneducated and low educated individuals, researchers have adopted age- and education-specific norms for older cohorts. In many countries, such as the USA (Crum et al., 1993), Finland (Ylikoski et al., 2009), Japan (Ishizaki et al., 1998), Korea (Han et al., 2008; Lee et al., 2002; Son, 2002), Spain (Contador et al., 2016), Portugal (Freitas et al., 2015), and Brazil (Bertolucci et al., 1994; Brucki et al., 2003; Laks et al., 2007), normative data are available based on particular sociodemographic variables. For example, Crum and colleagues (1993) created population-based norms (n=18,056) by age and educational level in the USA. They found that the median MMSE score was 29 for individuals with at least 9 years of schooling, 26 for those with 5 to 8 years of schooling and 22 for those with 0 to 4 years of schooling (Crum et al., 1993). Another example is the investigation of Kochhann and colleagues (2010), who defined new cut-off scores in a stratified sample (n=968) by four levels of education with the following values: 21 for the illiterate group (sensitivity=93%, specificity=82%), 22 for the low education group (1-5 years of schooling) (sensitivity=87%, specificity=82%), 23 for the middle education group (6-11 years of schooling) (sensitivity=86%, specificity=87%) and 24 for the high education group (≥ 12 years of schooling) (sensitivity=81%, specificity=87%) (Kochhann et al., 2010). Accordingly, for an Arabic-speaking Egyptian older population (n=159), new recommended cut-off scores were ≤ 21 for individuals with less than 9 years of education or who were illiterate and ≤ 22 for individuals with 9 or more years of education (ElKholy & Ore, 2018).

Many studies have reported disparity on MMSE performance among illiterate/uneducated individuals. For instance, in Brazil median scores of 18, 19 and 20 points (Bertolucci et al., 1994; Brucki et al., 2003; Laks et al., 2007) and a mean of 17.4 (SD=4.0) have been reported (Scazufca et al., 2009). Overall, MMSE cut-off scores for illiterate individuals in Brazil range from 13 to 21 (Kochhann et al., 2010; Vasconcelos et al., 2007). The aforementioned findings emphasize the heterogeneity of illiterate/uneducated and low educated groups. It also highlights the fact that, while normative data and different cut-off scores for these groups can be helpful, they may lead to misinterpretations of MMSE scores due to their multiplicity.

Versions of the MMSE for illiterate or low-educated individuals

Adapted versions of the MMSE have been developed in several countries for illiterate/uneducated or low literate individuals. Such countries are Brazil (MMSE-mo) (Brito-Marques & Cabral-Filho, 2004), China (CAMSE) (Xu et al., 2003), Turkey (MMSE-I) (Ertan, 1999), India (Hindi-MMSE) (Ganguli et al., 1995), Spain (MMSE-37) (Contador et al., 2016), and Bangladesh (BAMSE) (Kabir & Herlitz, 2000). In these versions, the items that were affected by education and literacy have been adapted, simplified, or omitted (Magklara et al., 2019). These changes include either substitution of reading and writing items with verbal commands and pictures/figures or exclusion of them, as well as simplification of drawing tasks (Ganguli et al., 1995; Shim et al., 2017; Verghese et al., 2012).

Revised Version of the MMSE: MMSE-2

Although the MMSE has been revised and the MMSE-2 is now available with new normative data, the effect of demographic variables on performance, especially among older (functional) illiterate/uneducated or poorly educated individuals, remains unaddressed. In fact, it has been found that individuals with higher levels of education have higher performance on average as compared with those with lower levels of education (Song et al., 2020). Also, one of the two new tasks that have been added to the revised form of the test, the extended version, is Story Memory (SM). SM has been found to be affected by age, educational level, and sex, as well as their interaction. Previous studies have shown that SM scores decline in older and low-educated populations (Song et al., 2020). Additionally, while no sex differences have been reported in verbal memory in individuals with a low educational level (e.g., 0-5 years of education), they have been observed in those with a higher educational level (12-15 years and 16 years or more). Song and colleagues (2020) developed stratified norms for SM-MMSE-2 based on a large population dataset (1.168 individuals), highlighting the necessity for identifying the role of demographic variables in performance (Song et al., 2020).

Given the publication of the MMSE-2, one might expect that the MMSE would be a test of relatively low interest for use in clinical and research settings given its known limitations. Also, presumably, neuropsychologists are aware of the documented disadvantages of traditional measures in the cognitive assessment of individuals with limited or no literacy/education, and most likely do not use a single instrument on which to base a diagnosis. Yet, this does not seem to be the case in many studies. Despite progress in cognitive screening (i.e., development of other instruments, such as the Rowland Universal Dementia Screening; (Araujo et al., 2018; Araujo et al., 2020; Goudsmit et al., 2021), the available data have shown that many tests have been inadequately validated to ensure diagnostic accuracy, especially for a diagnosis based on a wide range of cognitive functions, in (functionally) illiterate/uneducated or low-educated individuals (for a review, see Paddick et al., 2017) and inappropriate tests with inadequate norms are still often used both in research and in clinical practice.

Both the MMSE and the MMSE-2 are still widely used in clinical and research situations that demand rapid cognitive screeners (e.g., epidemiological studies, clinical assessments), unfortunately often without taking into account (functional) illiteracy/lack of education. In fact, in one epidemiological study, the MMSE is the only reference standard for a dementia diagnosis though illiterate individuals are included (Bich et al., 2019). When assessing potential memory impairment reflecting pathological changes in (functional) illiterate/uneducated or low educated older adults, however, we should bear in mind that the MMSE/MMSE-2 score is not a shortcut toward a dementia diagnosis (Song et al., 2020). In fact, even recent studies (which have used an education-specific cut-off point) have utilized the MMSE score as the only diagnostic criterion determining cognitive impairment and have based the selection/categorization of their participants solely on performance on this test

(Li et al., 2023a; Li et al., 2023b; Sun & Zhang, 2023). Another argument that the MMSE is still frequently used in individuals with or without schooling concerns the fact that new MMSE normative data have recently emerged in many countries. For example, the normative study for the population in Northern Italy (different from the prior normative data for Southern Italy only) (Mazzi et al., 2020) includes illiterate individuals as a separate category (Foderaro et al., 2022). Thus, the aforementioned studies indicate that awareness of the limits of the test and relevant recommendations regarding pitfalls in its use is not an outdated issue but continues to be essential. Furthermore, the choice of appropriate tests sensitive to cognitive impairment is also an important issue in COVID-19 research. Specifically, neuropsychological assessment is used to detect possible cognitive impairment resulting from COVID-19 (Bonizzato et al., 2022). Several studies consider the MMSE and the MoCA as acceptable and suitable measures to detect cognitive deficits in post-COVID-19 patients, whether or not premorbid conditions put them at risk for cognitive deficits (RCD +, RCD-) (Aiello et al., 2022; Bonizzato et al., 2022). Thus, it is clear that many investigators continue to use the MMSE without taking into account that low educated/(functional) illiterate/uneducated participants may be included, and that the use of these tests could lead to biased results relative to their cognitive status, hence, to false conclusions regarding the research hypotheses. Also, although the MMSE is often used in combination with one or more tests for cognitive screening, these other tests are usually traditional neuropsychological measures that have the same methodological issues as the MMSE and are prone to underestimating the abilities of low educated/(functional) illiterate/uneducated individuals. The fact that, despite the development of tests that reflect knowledge or activities typical of daily living, many epidemiological and other studies in several fields, as well as clinical assessments, continue to utilize traditional, commonly used neuropsychological tests, such as the MMSE, in a way that is not appropriate for an educationally heterogeneous population, poses major validity issues and raises questions to the research community regarding a matter that is well-known but often appears to be overlooked. The aforementioned evidence suggests that not only does the MMSE remain a test of great interest but also that a comprehensive approach is crucial for avoiding misleading results in a broader research field.

Limits and Recommendations

Numerous attempts and recommendations have been made by investigators in order to minimize or eliminate bias related to education and other socio-demographic variables on MMSE performance. Some authors have proposed addressing this issue by adjusting or correcting scores. Many studies support that adjusting cut-off points of traditional screening tests (particularly in different populations) according to years of education or educational level or in some cases, literacy, reduces false-positive results and can improve the utility of cognitive screening tasks such as the MMSE (Blesa et al., 2001; Brito-Marques & Cabral-Filho, 2004; Brucki et al., 2003; Kochhann et al., 2010; Ortega et al., 2019; Pedraza et al., 2012; Rosli et al., 2016; Woodford & George, 2007). Furthermore, Monroe and Carter (2012) advise considering the use of an age- and education-adjusted formula (Mungas et al., 1996) and being extra cautious when interpreting results in people over the age of 75 with less than 8 years of schooling (Monroe & Carter, 2012).

Other authors, however, argue that adjusting variables -- such as educational level -- with a causal link to dementia will significantly decrease validity by eliminating the validity effect (Kraemer et al., 1998) and lead to information loss (Pedraza et al., 2012), undermining the efficiency of screening and dementia assessment (Lee et al., 2014; Morris et al., 1996). Thus, the adjustment approach is considered by many ineffective (Carnero-Pardo, 2014; Carnero-Pardo et al., 2011). Additionally, this proposal has been considered problematic since it has led to discrepancies in clinical assessment due to the development of a wide variety of cut-off scores, even within the same country (Magklara et al., 2019). Yet another occurring problem when changing the cut-off point is that it alters both the sensitivity and the specificity of the MMSE, increasing one while decreasing the other (Tombaugh & McIntyre, 1992).

The approach of developing normative data based on socio-demographic variables is in general an acceptable and useful method, considering the association between (functional) illiteracy/lack of education and dementia. This practice, however, may mask early signs of cognitive decline (Kosmidis, 2018; Morris et al., 1996) and lead to confounding results relevant to determining impairment due to the plurality of norms even within the same country (e.g., Korea, Brazil, Italy) (Bertolucci et al., 1994; Brucki et al., 2003; Foderaro et al., 2022; Laks et al., 2007; Lee et al., 2002; Son, 2002).

With respect to the MMSE adapted forms, the counter argument is that although adaptations may improve a test's precision, at the same time they may also generate issues of psychometric validity and equivalence with the original test versions since there is the risk that it may be simplified or substantially changed (Ganguli et al., 1995; Magklara et al., 2019). In agreement with other researchers, Magklara, Stephan, and Robinson (2019) have suggested that test adaptations could lead to bias due to culture and language differences (e.g., Western vs non-Western populations), as some items may be problematic, not applicable, have limited relevance across different cultures, or may be difficult to translate in a meaningful way (Ganguli et al., 1995; Magklara et al., 2019; Mathuranath et al., 2004; O'Driscoll & Shaikh, 2017; Raina et al., 2013; Shim et al., 2017; Werner et al., 1999). Furthermore, relevant studies to date have shown that even on adjusted versions for illiterate/uneducated individuals, performance on most items of the MMSE is still associated with education. Rosselli and colleagues (2000) found that 16 out of 19 questions differentiate between uneducated and educated individuals (even those with one year of formal schooling) (Rosselli et al., 2000). Also, Brito-Marques, and Cabral-Filho (2004) compared illiterate individuals and individuals with 1 to 4 or 5 to 8 years of schooling from low and middle socio-economic levels on two versions of the MMSE (i.e., the MMSE adapted to the Portuguese language and the MMSEmo comprised adaptations of the copy and calculation items of the former). Based on their findings, individuals with more schooling performed better than those with less schooling on both adapted test versions (Brito-Marques & Cabral-Filho, 2004).

Regardless of their limitations, adapted forms and data normed specifically for illiterate/uneducated individuals based on sociodemographic variables are essential for assessing cognitive ability in poorly educated populations and offer a better diagnostic prospect compared to the original test and its recommended cut-off scores. Also, with respect to education, breaking down the categorization based not only on a dichotomous approach ["having no formal education (illiterate)"/"having formal education" (literate)], but also allowing for gradations (such as pure illiterate, semi-illiterate, low-level literate, high-level literate) would appear to increase the validity of normative data and cut-off scores (Kim et al., 2014). This suggestion has also been supported by a study that showed a major impact of education on the MMSE among different educational groups, whereas no differences were observed between uneducated and educated individuals (0 vs ≥ 1 year of education) (Kochhann et al., 2010). Moreover, along with educational level, functional illiteracy is a significant aspect that should be considered when adjusting cut-off scores, creating normative data, or interpreting performance on the MMSE (Brucki & Nitrini, 2010).

Reported findings demonstrate that illiterate/uneducated and low educated older populations are not a homogeneous group. Thus, their cognitive assessment may be associated with factors such as age, sex, language, culture, occupation, socio-economic status, and area of residence (urban vs. rural) in addition to education (Brucki & Nitrini, 2010; Evans et al., 2008). Therefore, these variables should be acknowledged further in the interpretation of results, in adapted versions, or when correcting cut-off scores for the MMSE.

One of the most important suggestions regarding the use of the MMSE with illiterate/uneducated and low educated individuals is to administer other cognitive tasks or scales for detecting cognitive impairment as well (Reisberg, 2007). In fact, rarely is a single screening test used as a basis for a diagnosis (in addition to a neurological exam), as a comprehensive neuropsychological assessment is usually required. An alternative suggestion for early detection of cognitive decline in these two populations is to base clinical suggestions not on the total score, but on the domains that have been found to be less affected by education on the MMSE (i.e., memory), in combination with performance on other psychometric tests or functional scales (Matallana et al., 2011; Shyu & Yip, 2001). Lastly, Crum and colleagues (1993) proposed that MMSE scores should only be used to identify current cognitive difficulties and not to make formal diagnoses (Crum et al., 1993).

In contrast to reformative methods and recommendations, an increasing number of researchers have critiqued and rejected the MMSE as an inappropriate screening tool for the detection of cognitive decline in individuals with low educational or literacy level, suggesting that no modifications can improve its diagnostic accuracy. Specifically, some have suggested that it should not be used with individuals with less than 5 years of schooling (Cruz-Orduna et al., 2012; Evans et al., 2008; Ostrosky-Solis et al., 2000; Scazufca et al., 2009; Zunzunegui & Otero, 2010). Given that uneducated/(functional) illiterate individuals may perform as well as educated/literate individuals in coping with tasks representing activities encountered in daily life (Kempler et al., 2010; Reis et al., 2001), the need for replacing traditional neuropsychological tests with new tests with construct validity becomes apparent.

Similar points of view have been expressed for other traditional tests, as well. Researchers question the use of formal screening tools, including the MMSE, while judging them as unreliable for poorly educated individuals, recommending their substitution with new tests with construct validity. In some cases, the rejection of traditional methods has led to attempts to examine a patient's performance indirectly via an interview with a caregiver, but the use of second-hand information to assess performance may prove to be inaccurate (Goudsmit et al., 2021). Interviewing a caregiver is common practice among clinicians, when possible, usually gathering medical and other relevant background information (e.g., family, medical, level of functioning); thus, it should be used along with selected screening tests as supplementary information for clinical diagnosis.

Finally, we should bear in mind that, uneducated individuals are further at a disadvantage relative to those who have received formal education, due to lack of test familiarity and test-wiseness (Nell, 1999). Also, the MMSE is a test that, like many other traditional tools, requires paper and pencil responses. Thus, people who have not received formal schooling may decline to perform the tasks (Carnero-Pardo, 2014). Hence, the MMSE should not be the only screening instrument for dementia or cognitive decline in this population.

Conclusions

The MMSE is one of the most popular screening scales for cognitive impairment, especially among the elderly. Its appropriateness as a measure for detecting dementia or cognitive decline in illiterate/uneducated and low educated individuals is a long-recognized controversial topic among researchers. Based on the literature, it has been well documented that education is a strong predictor of performance on the MMSE and that other socio-demographic factors should also be considered during clinical assessment of illiterate/uneducated or low educated older adults. Specifically, among the parameters that one should consider when administering the MMSE, especially in illiterate/uneducated or low educated groups, are the following: educational level, literacy and functional (il)literacy, language/ethnicity and cultural background, socioeconomic status/occupation, previous history (medical/environmental), area of residence, sex, and age. Additionally, many researchers have endorsed the development of normative data, and adaptation and validation of the MMSE in each country and language and diverse environments as essential steps to reduce the false-positive rate for cognitive impairment in low educated people (Brucki & Nitrini, 2010; Vasconcelos et al., 2007; Magklara et al., 2019; Ortega et al., 2019). In fact, some authors have suggested that it is desirable to reappraise the validity of the MMSE each time it is used in a new population (Brito-Marques & Cabral-Filho, 2004). In conclusion, while the MMSE is not the optimal assessment method for detecting dementia or cognitive decline in illiterate/uneducated and low educated individuals, awareness of its limitations and relevant recommendations for its appropriate use is crucial for accurate and meaningful interpretation when the test is used.

In summary, we propose the following recommendations for improving diagnostic accuracy when administering the MMSE to illiterate/uneducated and low educated individuals:

1. Use adapted versions of the test, that meet the requirements, based on country/environment (Brito-Marques & Cabral-Filho, 2004; Contador et al., 2016; Ganguli et al., 1995; Kabir & Herlitz, 2000; Magklara et al., 2019; Xu et al., 2003).
2. Develop normative data (discrete norms or regression-based norms) according to socio-demographic variables using multiple stratification including (functional) illiteracy/lack of education (Crum et al., 1993; Freitas et al., 2015; Kochhann et al., 2010; Lee et al., 2014; Vasconcelos et al., 2007).
3. Adjust or correct cut-off scores (appropriate to the target populations) (Blesa et al., 2001; Brito-Marques & Cabral-Filho, 2004; Brucki et al., 2003; Brucki & Nitrini, 2010; Kochhann et al., 2010; Ortega et al., 2019; Pedraza et al., 2012; Rosli et al., 2016; Woodford & George, 2007).
4. Make the most of information by cognitive domains, not only total score (Crane et al., 2006; Matallana et al., 2011; Shyu & Yip, 2001).
5. Determine impairment using the MMSE in conjunction with other tests/scales (Aprahamian et al., 2011; Shyu & Yip, 2001) that are not school based but are relevant to daily activities (Ortega et al., 2019), as well as administer a short reading and writing test to check for (functional) illiteracy and gather further information by a caregiver (Goudsmit et al., 2021).

6. Interpret MMSE scores with caution (particularly in older and illiterate/uneducated or low educated individuals) (Monroe & Carter, 2012), while retaining awareness of the factors that may cause bias and the limitations of the test.
7. Apply a combination of the aforementioned methods.
8. Avoid administering the MMSE to individuals with no schooling or less than 5 years of schooling (Carnero-Pardo, 2014; Cruz-Orduna et al., 2012; Evans et al., 2008; Ostrosky-Solis et al., 2000; Rosselli et al., 2000; Scazufca et al., 2009; Zunzunegui & Otero, 2010).
9. Create an equivalent adapted version of the MMSE for illiterate/uneducated individuals by using a visual format that is appropriate for their needs (e.g., use of props/physical objects such as coins or other everyday items).

Our study has many strengths. We highlight fundamental questions regarding one of the most widely used screening tests and other relevant tasks (i.e., verbal/visual memory tests, visuospatial and verbal ability tests, tests that assess processing speed and executive functioning) that need to be reconsidered for our current toolkit for the neuropsychological assessment of the (functionally) illiterate/uneducated population. The fact that the limits and recommendations related to the interpretation of the MMSE apply to many school-based neuropsychological tests, including the MMSE-2 and the MoCA (Gómez et al., 2013), makes our study relevant to initiatives such as that of the American Academy of Clinical Neuropsychology 2050 project, as it underlines ways of improving cognitive assessment of (functionally) illiterate/uneducated or low-educated individuals. In the context of fair testing and making neuropsychological tests more meaningful for (functionally) illiterate/uneducated or low-educated individuals, the aforementioned guidelines could contribute to finer discrimination between cognitively healthy and impaired individuals in this population. Hence, a theoretical discussion based on comprehensive information concerning the use of the MMSE/MMSE-2 in the cognitive assessment of individuals with no or limited education/literacy could enhance research methods and reduce bias against these groups.

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ΒΙΒΛΙΟΓΡΑΦΙΚΗ ΑΝΑΣΚΟΠΗΣΗ | REVIEW PAPER

Σύντομη εξέταση της νοητικής κατάστασης σε αναλφάβητα άτομα και σε άτομα με χαμηλό εκπαιδευτικό επίπεδο: Περιορισμοί και προτάσεις

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ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ	ΠΕΡΙΛΗΨΗ
Αναλφάβητα άτομα, Χαμηλό εκπαιδευτικό επίπεδο, Σύντομη εξέταση της νοητικής κατάστασης, Προτάσεις	Η αύξηση του προσδόκιμου ζωής συσχετίζεται με αύξηση του αριθμού των ηλικιωμένων ατόμων τα οποία διαγιγνώσκονται με άνοια. Με βάση το γεγονός ότι τα άτομα με χαμηλό εκπαιδευτικό επίπεδο/χωρίς εκπαίδευση συχνά αποτελούν την πλειονότητα ερευνητικών δειγμάτων ηλικιωμένων, καθίσταται επιτακτική η ανάγκη να αναγνωριστούν -ή/και να δημιουργηθούν εκ νέου- κατάλληλες νευροψυχολογικές δοκιμασίες για την πρόωπη ανίχνευση και τη διάγνωση γνωστικής έκπτωσης στη συγκεκριμένη ομάδα. Δεδομένου ότι αρκετές νευροψυχολογικές δοκιμασίες υποεκτιμούν τις γνωστικές δεξιότητες των αναλφάβητων ατόμων και των ατόμων με χαμηλό εκπαιδευτικό επίπεδο, η χορήγησή τους σε αυτές τις ομάδες χρήζει επανεξέτασης ή απαιτείται αναθεώρηση της μορφής τους. Ένα ευρέως χρησιμοποιούμενο διεθνώς εργαλείο κατά την κλινική εκτίμηση είναι η Σύντομη Εξέταση της Νοητικής Κατάστασης. Η εκπαίδευση αποτελεί σημαντικό προβλεπτικό παράγοντα της επίδοσης σε αυτή τη δοκιμασία, ως εκ τούτου, παρατηρείται διαφωνία μεταξύ των ερευνητών σχετικά με τη χρήση της σε πληθυσμούς με χαμηλό εκπαιδευτικό επίπεδο/χωρίς εκπαίδευση. Προκειμένου να μειωθεί η επίδραση της εκπαίδευσης, καθώς και άλλων παραγόντων, στην επίδοση, είναι διαθέσιμο ένα ευρύ φάσμα ερευνητικών προτάσεων, ωστόσο, αρκετοί μεθοδολογικοί περιορισμοί παραμένουν και κάποιοι νέοι έχουν προκύψει αναφορικά με τη χορήγηση της δοκιμασίας σε αναλφάβητα άτομα ή σε άτομα με χαμηλό εκπαιδευτικό επίπεδο. Στην παρούσα μελέτη, παρουσιάζουμε μια επισκόπηση των δυσκολιών που προκύπτουν κατά τη χρήση και ερμηνεία της επίδοσης της Σύντομης Εξέτασης της Νοητικής Κατάστασης, τις προτάσεις χορήγησης και τους περιορισμούς που ανακύπτουν εξ αυτών, καθώς επίσης, υπογραμμίζονται οι βέλτιστες μέθοδοι χρήσης της κλίμακας για την κλινική εκτίμηση ατόμων με χαμηλό εκπαιδευτικό επίπεδο/χωρίς εκπαίδευση.
ΣΤΟΙΧΕΙΑ ΕΠΙΚΟΙΝΩΝΙΑΣ	
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