Validity and Reliability Studies of Modified Mini Mental State Examination (MMSE-I) For Turkish Illiterate Patients with Diagnosis of Alzheimer Disease

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SUMMARY

Objective: To investigate the validity and reliability of modified Mini Mental State Examination (MMSE-I) for illiterate patients in a Turkish population with Alzheimer's disease (AD).

Material and Method: A total of 107 illiterate patients with Alzheimer's disease (women: 65, men: 42) and 68 illiterate healthy volunteer subjects (women: 36, men: 32) were included in the study. MMSE-I and Geriatrics Depression Scale were performed on all subjects, Alzheimer patients were also administered Basic Activities of Daily Living (B-ADL). The Clinical Dementia Rating (CDR) was used to determine the severity of disease, while a receiver operating characteristic (ROC) analysis was performed to analyze the cut-off scores of MMSE-I and the positive/negative predictive values that were calculated for the optimal cut-off scores. Internal consistency was measured using Cronbach's coefficient $\alpha$. Additionally, correlations between total MMSE-I score and the CDR, B-ADL, and GDS scores were examined.

Results: The MMSE-I scores significantly and inversely correlated with CDR (-0.82, p=0.000) and B-ADL scores (-0.051, p=0.000). The optimal cut-off points of MMSE-I were 23/24, which yielded a sensitivity of 99.0% - %100.0, a specificity of 98.5% - 97.0%, and an AUC of 1.0/1.0, respectively. Reliability of the MMSE-I was high ($\alpha = 0.70$).

Conclusion: The total MMSE-I score was able to differentiate the AD group from the control group.

Key Words: Alzheimer's disease, MMSE-I, illiterate, validity, reliability

INTRODUCTION

Alzheimer’s disease (AD) is a neurodegenerative dementia characterized by an impairment of cognitive functions, including memory along with disturbances in language, attention, executive functions, gnosis, and praxis (Geldmacher et al. 1997, Hannay et al. 2004). The prevalence rate of AD is 10% around the age of 65, and increases to 50% in those over 85 years of age (Evans et al. 1989, Corrada et al. 2010). According to the TUIK data, those over 65 years of age present 7.3% of the Turkish population, which corresponds to an elderly population of approximately 6.48 million individuals. In rural areas, a larger proportion of illiterate subjects can reach over 45% among the elderly (TUIK, 2011).

A higher occurrence of cognitive disorders including AH in illiterate populations or in subjects with low level of education is a well-established phenomenon (Prencipe et al. 1996, Lee et al. 2008). However, the battery of neuropsychiatric tests that are extensively used are not only for the diagnosis, but also for prognostic estimations and for assessing the response to treatment in AD. These have been specifically developed...
for Western populations with a relatively higher educational level, which results in a potential increase in the rate of misdiagnosis when administered to illiterate individuals (Yassuda et al. 2009).

MMSE (MMT; MMSE: The Mini Mental State Exam) is a test of cognitive impairment developed for educated individuals, and is commonly used worldwide (Folstein et al. 1975). The validity and reliability of MMSE for Turkish individuals with mild dementia and at least 5 years education at the primary level have been previously demonstrated by Güngen et al. (Güngen C et al. 2002). However, little is known about the validity and reliability of the revised MMSE (MMSE-I) developed for illiterate populations by same authors (Ertan et al. 1999).

In this study, we aimed to investigate the validity and reliability of modified Mini Mental State Examination (MMSE-I) for illiterate patients in a Turkish population with Alzheimer’s disease (AD).

METHOD

INSTRUMENTS

1. MMSE-I

The version of MMSE developed by Ertan et al. for illiterate individuals (MMSE-I) has been used for study purposes (Ertan et al. 1999). The score range of MMSE-I was 0 to 30. (Appendix 1)

Subscales

• Orientation

  o Orientation to time: (5 points) In this part, the question “what day of the month is it?” in the version for the educated has been replaced by the question “what part of the day is it?”. Other questions included “year”, “season”, “day of the week”, and “month”.

  o Orientation to place: (5 points) The questions in this section included “what country are we in?”, “what district are we in?”, “what hospital-building are we in?” and “what floor of the building are we on?”.

  (Due to a high number of participants who had a difficulty in comprehending the question “what country are we in?” or “what is the name of our country?”), tips such as “Are we in Germany now?” have been provided. Participants also had a disposition to articulate the name of the city they were born when they were asked the question “what city are we in?”, thus tip was again provided by questions such as “Is this the city you were born?”.

• Words registration: (3 points) This section was the same as the version for the educated. A total of 3 different words (blue, hawk, tulips) were presented to the subject with a second interval, and he/she was asked to repeat these three words. If the participant was unable to repeat all these 3 words in the first try, the same words were pronounced for two more times at most. Each correct recall was given 1 point irrespective of the repeat order. The patient was told that he/she would be asked to repeat the same words after a few minutes.

• Attention: (5 points) In this part, the patient was asked to count the days of the week in the reverse order. For each correct day 1-point was given provided that the patient was able to count a minimum of 5 days in the reverse order.

(In case the patient was unable to understand the instructions, an example was provided. For example: Sunday was preceded by Saturday, and what Saturday was preceded by etc.)

• Words recall: (3 points) The patient was asked to recall the 3 words (blue, hawk, tulips) that he was asked to remember in the registration memory section. Each correct answer was given 1-point irrespective of the order. The words could also be presented in a multiple-choice format or tips could be given to help the participants. However, these were considered in the statistical assessments.

• Language: (8 points) The “naming”, “repeating” and “comprehension” subscale were the same as in the version for the educated subjects. For naming subscale, the participant was asked to name two familiar objects (watch and pen). In the repeating subscale, the participant was asked to repeat a sentence (I would have gone if he had gone) right after the interviewer. Care was experienced not to be too quick or slow when saying the sentence. In the comprehension subscale, a 3-step instruction was given (take the piece of paper with your [non-dominant] right/left hand, fold it in the middle with both hands, and put it on the floor) and 1-point was given for each correct step. Instead of the “writing” subscale for educated participants, the participant was asked to talk about his/her house and a 30 second time-period was allowed, during which 1-point was given for each meaningful sentence. However, due to frequent failure, a sample sentence was given to the participants. As a replacement for the “reading” subscale, first the interviewer asked the participant to repeat what the interviewer was doing after looking his/her face and then the interviewer closed his/her eyes.

• Visuospatial functions: (1 point) The patient was initially shown a figure consisting of two squares one within the other (Appendix 1), and then asked to copy it while he/she was allowed to look at the figure.
MMSE-I
-THE MODIFIED MINI MENTAL STATE EXAMINATION FOR ILLITERATE PATIENTS-

Name: Date:  
Age: Job:  
Education (years): Handness:

<table>
<thead>
<tr>
<th>TOTAL SCORE</th>
</tr>
</thead>
</table>

**• ORIENTATION**

<table>
<thead>
<tr>
<th>TIME</th>
<th>PLACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Year :</td>
<td>☐ Country :</td>
</tr>
<tr>
<td>☐ Mon :</td>
<td>☐ City :</td>
</tr>
<tr>
<td>☐ Part of the day :</td>
<td>☐ District :</td>
</tr>
<tr>
<td>☐ Day of the week :</td>
<td>☐ Hospital :</td>
</tr>
<tr>
<td>☐ Season :</td>
<td>☐ Floor :</td>
</tr>
</tbody>
</table>

**• REGISTRATION**

☐ Blue  ☐ Hawk  ☐ Tulips  
/Register the number of trials/

**• ATTENTION**

Ask the patient to count the days of the week in the reverse order. *(For example: Sunday is preceded by Saturday, and what is Saturday preceded by.)*

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

**• RECALL**

☐ Blue  ☐ Hawk  ☐ Tulips  
/*Category cue:*

/*Multiple choice:*
2. Geriatric Depression Scale

Presence of depression was examined using the 15-item short form (GDS-15) (Burke et al. 1991) of the “Geriatric Depression Scale” developed by Yesevage (Yesavage et al. 1982). In this scale, a total score between 0 and 4 was considered normal, while scores between 5-8, 9-11 and 12-15 indicate the presence of mild, moderate, or severe depressive symptomatology.

3. Clinical Dementia Rating Scale

“Clinical Dementia Rating Scale” (CDR) was used to estimated the stage of the disease (Hughes et al. 1982). In this test which examines 6 domains: memory, orientation, judgment and problem solving, social functioning outside home, home and hobbies, and personal care, staging was performed as follows: "*0: Normal aging, *Stage 0.5: Mild Cognitive Impairment,*Stage 1: Mild dementia, Stage 2: Severe dementia.

4. Basic Activities of Daily Living Scale

The “Basic Activities of Daily Living Scale (B-ADL)” developed by Katz et al. was used to estimate the effect of the cognitive impairment on daily activities of living (Katz et al. 1963). The 6-item version of the index was used in our study to assess the following areas: *feeding, *dressing, *moving in and out of the bed, *toileting, *bathing, and *incontinence. Independence was given a “0” point in basic activities of daily living, while requiring assistance was given a score of “1” and if the patient is not independent at all he/she was given a score of “2”.

• VISUOSPATIAL FUNCTIONS

COPYING

☐ Ask the subject to copy the following shape.

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GERIATRIC DEPRESSION SCALE (GDS-15) (Burke et al. 1991) of the “Geriatric Depression Scale” developed by Yesevage (Yesavage et al. 1982). In this scale, a total score between 0 and 4 was considered normal, while scores between 5-8, 9-11 and 12-15 indicate the presence of mild, moderate, or severe depressive symptomatology.

CLINICAL DEMENTIA RATING SCALE (CDR) was used to estimated the stage of the disease (Hughes et al. 1982). In this test which examines 6 domains: memory, orientation, judgment and problem solving, social functioning outside home, home and hobbies, and personal care, staging was performed as follows: "*0: Normal aging, *Stage 0.5: Mild Cognitive Impairment,*Stage 1: Mild dementia, Stage 2: Severe dementia.

BASIC ACTIVITIES OF DAILY LIVING SCALE (B-ADL)” developed by Katz et al. was used to estimate the effect of the cognitive impairment on daily activities of living (Katz et al. 1963). The 6-item version of the index was used in our study to assess the following areas: *feeding, *dressing, *moving in and out of the bed, *toileting, *bathing, and *incontinence. Independence was given a “0” point in basic activities of daily living, while requiring assistance was given a score of “1” and if the patient is not independent at all he/she was given a score of “2”.

---

* NAMING

☐ Pen
☐ Watch

* REPEATING

☐ Ask the asked to repeat this sentence “I would have gone if he had gone”

* COMPREHENSION

☐ Ask the patient to take the piece of paper with his/her [non-dominant] right/left hand
☐ Fold it in the middle with both hands
☐ Put it on the floor
☐ Ask the patient to talk about his/her house (30 second time-period was allowed)
☐ Ask the patient to repeat what the interviewer is doing after looking his/her face and then the interviewer closed his/her eyes.

* VISUOSPATIAL FUNCTIONS

COPYING

☐ Ask the subject to copy the following shape.
Incontinence was scored as follows: 0: absent, 1: once or twice a week, 2: three times or more weekly. B-ADL score between 0 and 4 was considered as independence in daily living activities, while a score between 5 and 8 showed semi-independence, and 9 and 12 as complete dependency. Instrumental Daily Living Activities were not assessed in our study.

PARTICIPANTS

A total of 107 illiterate patients attending to the Neurology and Geriatric Outpatient Units, Medical Faculty of Bezmialem University and diagnosed as having Alzheimer’s disease based on NINCDS-ADRDA diagnostic criteria were included in our study. Also a total of 68 healthy individuals were also included as controls. No age limit was applied for patients with Alzheimer’s disease. MMSE-I and short form of the Geriatric Depression Scale (GDS-15) were administered to all participants; B-ADL was also administered to individuals in the patient group and the disease was staged according to CDR. The two groups were compared in terms of MMSE-I total and cognitive subscale scores, GDS, age, gender and hand dominance. Patients who could read and/or write only without a formal education were excluded. Majority of the control subjects were patients’ relatives or individuals from the same district who were illiterate.

STATISTICAL ANALYSES

ROC (Receiver Operating Characteristic) analysis was performed to determine the cut-off point that could discriminate normal individuals and AD patients and positive and negative predictive values (PPV and NPV) were estimated for this cut-off point. For the reliability of MMSE-I, each subscale was included in the analysis as a variable and the Cronbach alpha coefficient was calculated. The correlation between MMSE-I and CDR, B-ADL and GDS was explored. The effect of age (> 65 years vs. ≤ 65 years) and gender on the tests was examined using Mann-Whitney Test. Also, a Spearman correlation analysis was performed to examine the correlation between each subscale for cognitive functions and the total MMSE-I score.

RESULTS

The average age was 70.7 years among AD patients (range: 47-83 y; SD ± 6.6) and 69.1 years (range: 55-83y, SD: ± 6.5) among controls. The female to male ratio was 52.9% to 47.1%, and 60.7% to 39.3% among AD patients and controls, respectively. There were no significant differences between AD and control groups in terms of age, gender, and dominant hand. The total MMSE-I scores in the two groups were compared using Mann-Whitney test, with significantly higher scores among controls than in AD patients: 28 (IQR 3) vs. 15 (IQR 7), respectively (p < 0.001) (Table 1). The cut-off MMSE-I score that could help differentiate AD patients from controls was determined using a ROC analysis. Accordingly, the cut-off point for the total MMSE-I score was 23/24 based on a maximum sensitivity (99.0/100.0), specificity (98.5/97.0) and area under curve (1.0) results. The positive and negative predictive values for these cut-off points were 0.99/0.98 and 0.98/1.00, respectively (Table 2). Also, the correlation between the total MMSE-I score and each subscale of the cognitive domain for this cut-off value was explored. In this regard, highest and lowest correlations with the total MMSE-I score were observed for “orientation” and “registration memory”, respectively. Male and female patients did not differ significantly in terms of total MMSE-I score, GDS, B-ADL, and CDR stage. Only the average registration memory scores of MMSE-I were significantly higher in male patients as compared to females (p < 0.004). Among AD patients, only patients less than 65 years of age had significantly lower scores in the visual spatial domain (p < 0.04) (Table 3). As depicted in Table 4, there was a significant negative correlation between total MMSE-I scores and CDR (r=-0.82, p=0.000) and B-ADL (r=-0.51, p=0.000). However, total MMSE-I score did not correlate with age and GDS.

Of the patients in the AD group 21, 73, and 13 subjects had stage 1, 2, and 3 CDR, respectively. Patients with a CDR score of 0.5 were excluded. In order to test the internal consistency of MMSE-I, a reliability analysis was performed where each of the subscale were included in the analysis as variables. This has yielded a

### Table 1. Subject comparisons regarding age, gender, hand dominance and MMSE total scores among Alzheimer and control groups

<table>
<thead>
<tr>
<th></th>
<th>AD Group (AG)</th>
<th>Control Group (CG)</th>
<th>AG vs CG p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs (mean ± SD) (min-max)</td>
<td>70.0 ± 6.6 (47-83)</td>
<td>69.1 ± 6.5 (55-83)</td>
<td>p = 0.1</td>
</tr>
<tr>
<td>Gender (F/M %)</td>
<td>52.9/47.1</td>
<td>60.7/39.3</td>
<td>p &gt; 0.1</td>
</tr>
<tr>
<td>Hand dominance (R/L, %)</td>
<td>98.1/1.9</td>
<td>97.1/2.9</td>
<td>p &gt; 0.6</td>
</tr>
<tr>
<td>MMSE-E total score (median/IQR) (min-max)</td>
<td>15/7 (5-24)</td>
<td>28/3 (23-30)</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>

### Table 2. Sensitivities, specificities, PPV and NPV in different settings of cutoff values (ROC - AUC=1.00 p < 0.001)

<table>
<thead>
<tr>
<th>MMSE-I (Cut-off point)</th>
<th>SENSITIVITY</th>
<th>SPECIFICITY</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>97%</td>
<td>100</td>
<td>1.00</td>
<td>0.96</td>
</tr>
<tr>
<td>23</td>
<td>99%</td>
<td>98.5%</td>
<td>0.99</td>
<td>0.98</td>
</tr>
<tr>
<td>24</td>
<td>100%</td>
<td>97%</td>
<td>0.98</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Cronbach alpha coefficient of 0.70, which was considered to demonstrate the statistical reliability of the scale.

DISCUSSION

In this study of reliability and validity involving an illiterate population, MMSE-I was found to successfully differentiate between individuals with Alzheimer’s disease and individuals with normal cognitive functions.

Certain subscales of MMSE developed for educated individuals, particularly those addressing the cognitive functions of orientation, calculation, recall, read and write may be associated with misleading results in illiterate populations (Lou et al. 2007). A literature search for the studies examining the reliability and validity of MMSE in illiterate populations not only reveals a scarcity of such research, but also indicates low sensitivity (50%) and cut-off (17) values (Ostrosky-Solis F et al. 2000).

Undoubtedly, a modified form of MMSE specifically designed for illiterate populations may result in better diagnostic yield than that study, only few versions of MMSE for the uneducated have been encountered in the literature. Since education is known to have minimal influence on functions of naming, understanding a 3-step instruction, recall, and registration memory, the main focus in these studies included the modifications in the domains of attention, language, and visual-spatial function (Xu G et al. 2003, Brito-Marques PR et al. 2004, Laks J et al. 2007, Laks J et al. 2010).

In this study, a modified version (MMSE-I) developed by Ertan et al. was used without any alterations. The modifications performed by these authors involved the subscale on orientation for time and place, attention, read and write section of language, and visual-spatial functions. We propose that such a modification may be associated with certain shortcomings as compared to the version of MMSE for educated individuals. However, the performance in modified domains obviously correlates with the educational level, and the use of the original test will inevitably lead to misinterpretation of the test results in terms of the diagnosis.

A CDR stage of 0.5 has been thought to represent a condition referred to as “Mild Cognitive Impairment” (MCI). Individuals with a CDR stage of 0.5 were excluded on the basis that MMSE has a very low sensitivity and specificity for MCI, even in the educated.

Presence of depressive symptoms has been associated with an increased risk of AD in the elderly and with an accelerated cognitive worsening in those already diagnosed with AD. But again all these results are based on studies involving individuals with a certain level of education (Prince M et al. 1996, Geerlings MI et al. 2000, Wilson RS et al. 2004). In our study involving uneducated subjects, however, no correlation between GDS score and the total MMSE-I score.

The high correlation observed between MMSE-I and CDR and B-ADL (-0.82, p=0.000; and -0.51, p=0.000,
respectively), which are used to differentiate between AD patients and normal individuals, is an indication for the reliability and validity of the test. The sensitivity and specificity of the most appropriate cut-off value (23/24) determined by ROC curve in our study was higher than those reported both for the modified MMSE extensively used in current practice (Tombaugh TN et al. 1996) and for the study examining the reliability and validity of MMSE in a Turkish population (Güngen C et al. 2002). Again, these observations suggest that MMSE-I is a screening test with high validity for illiterate populations.

MMSE-I subscales were included as variables in the reliability analysis, with a satisfactorily high internal-consistency coefficient (Cronbach α: 0.77). This was interpreted as an indication for the high reliability of MMSE-I in terms of its ability to differentiate between AD patients and normal individuals.

Since neuropsychological assessments suggest that each cognitive domain may represent a specific function, a different cognitive subscale may be affected in the early course of the condition. In this regard, recall memory is particularly expected to show deterioration at the initial phase of the condition. In our study, the correlations between the total MMSE-I score and the subscale of cognition were explored. Despite correlations existing between the total score and all subscale score, orientation showed the highest level of correlation.

Literature data in educated populations suggest that although age may influence the results of neuropsychiatric tests, gender effect is negligible (O’Connor et al. 1989, Koivisto K et al. 1992, Tangalos EG et al. 1996). Despite significantly higher total MMSE-I and attention scores among those over 65 years of age, the groups did not differ significantly with respect to GDS, CDR, B-ADL, and other subscale of cognition in our study. Interestingly, AD patients as well as control subjects experienced a certain amount of difficulty in attention, which is consistent with literature reports (Rosselli M et al. 2006). In terms of gender, only a higher recall memory subscale score was higher among male participants than in female participants among MMSE-I subscale.

One limitation of our study was the inclusion of a smaller number of controls than AD patients. Also, only the education level was considered as inclusion criteria. However, the education level, in addition to several other factors such as occupation, sociocultural environment, and economic status were known to have an impact on cognitive functions (Brucki SMD et al. 2010). No sub-group analyses were performed in our study to take these factors into consideration. Another limitation relates to the absence of validation and reliability studies in Turkey for GDS, CDR, and B-ADL, all of which were used in our study.

In summary, this study showed that the new version of the MMSE (MMSE-I) for uneducated individuals can effectively determine the reliability and validity in differentiating dementia patients from individuals with normal cognition. Therefore, our study concludes that it may be used for the diagnosis and follow-up of patients with dementia.

REFERENCES


