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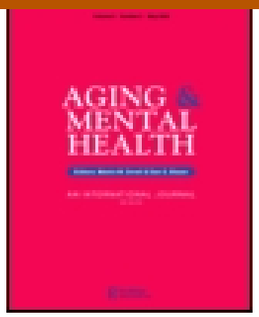

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Adapted MMSE and TYM cognitive tests: how much powerful in screening for Alzheimer's disease in Iranian people

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ABSTRACT

Alzheimer's disease (AD) is a major global health priority and providing an efficient way for early diagnosis of people developing dementia is important. The Mini-Mental State Examination (MMSE, total score = 30) and Test Your Memory (TYM, total score = 50) are widely used as screening tests for cognitive function. In the present study 174 subjects including healthy people (CON group) and those having Alzheimer's disease (AD group) were introduced to MMSE and TYM cognitive tests adjusted to Iranian population. Sensitivities and specificities with optimal cut-off scores, area under curve (AUC), positive predictive value (PPV) and negative predictive value (NPV) were measured for both tests. The MMSE scores of the CON and AD groups were 23.77 ± 0.327 and 10.88 ± 0.762, respectively. The TYM scores were 44.32 ± 0.389 and 14.37 ± 1.368 in the CON and AD participants, respectively. Findings in the MMSE test were: AUC = 0.962, optimal cut-off score = 18.5, sensitivity = 0.90 and specificity = 0.96. Values in the TYM test were: AUC = 0.991, optimal cut-off score = 31, sensitivity = 0.90 and specificity = 1. We found no correlation between the cognitive performance and age in the CON group but a positive correlation in the AD patients. On the other hand, t-test analysis indicated that achievement of the test scores are significantly sex dependent, with more scores attained by the females. Taken together, in regard to correct classification rate (CCR); the TYM test seems to be more appropriate for cognitive screening in our study. However, considering an analogous AUC, both tests are comparable and have high sensitivity and specificity for discriminating between people with and without AD.

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Alzheimer's disease; dementia; MMSE; TYM

Introduction

Cognitive problems are a feature of many neurological and medical diseases including stroke, Parkinson's disease, head injury, and epilepsy (Brown, Pengas, Dawson, Brown, & Clatworthy, 2009). According to the World Alzheimer Report ('2018 Alzheimer's disease facts and figures', Alzheimer's Association, 2018), 46.8 million people worldwide have dementia, and this number is expected to increase to 74.7 million by 2030. More than 35 million people have AD with a deterioration of memory and other cognitive domains that leads to death within 3 to 9 years after diagnosis. Although AD is not necessarily the outcome of aging; nevertheless, evidence shows the principal risk factor for AD is age and the diagnosis of AD after 85 years of age exceed one in three. The incidence of the disease doubles every 5 years after 65 years of age.

Patients with AD typically present with symptoms caused by poor recall of recently learnt visual and verbal materials so that clinical testing reveals episodic memory deficits (Greene, Baddeley, & Hodges, 1996; Nestor, Scheltens, & Hodges, 2004). Patients presenting with these symptoms and signs are diagnosed as having amnesic mild cognitive impairment (aMCI) if their problems are mild (with intact functional abilities) (Albert et al., 2011) or probable AD if they have problems which impact on their lives (McKhann et al., 2011). Many patients with aMCI progress to AD (Dubois & Albert, 2004).

Dementia affects each person differently and also has a significant impact on families and caregivers (Connell, Boise, Stuckey, Holmes, & Hudson, 2004). Early diagnosis of cognitive impairment may increase the chance of a slower progression of the disease (Leifer, 2003) and make target interventions before the progressive disease is established (Petersen et al., 2001). However, in milder cases, the diagnosis of AD is more difficult and may remain unclear after initial assessment. There has been a growing clinical and research interest in the early identification of people at risk of developing dementia. Actually, early accurate diagnosis of AD is a major global health priority (Petersen et al., 2009). Recently, numerous studies have attempted to identify a prognostic predictor of AD by using artificial neural networks (Mecocci et al., 2002), brain magnetic resonance imaging (Kanetaka et al., 2008; Tanaka, Hanyu, Sakurai, Takasaki, & Abe, 2003), single-photon emission computed tomography (Hongo et al., 2008) and cognitive function tests (Saumier et al., 2007). Although all of these are useful, however, disadvantages such as technical dependence, high costs, contrast-agent related allergies, potential

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exposure to radionuclide irradiation, requiring referral to specialists and taking time have limited their clinical application (Tsai et al., 2015).

A large number of cognitive screening instruments are available for the assessment of patient complaints of poor memory or cognitive impairment (Tate, 2010); however, none of them meets the three critical requirements for widespread use by a non-specialist that is, taking minimal operator time to administer, testing a reasonable range of cognitive functions and sensitive to mild AD (Brown et al., 2009). Further, dementia screening tools should be brief, easy to use and valid in different cultures and across elderly with various educational backgrounds (Lorentz, Scanlan, & Borson, 2002). Conclusively, there is a need for simple, quick and sensitive cognitive tests that provide a more efficient way of identifying people with dementia (National Collaborating Centre for Mental Health, 2007).

A short standardized mental status examination is helpful for the assessment of cognitive function in subjects with memory impairment (Folstein, Folstein, & McHugh, 1975). Short cognitive tests can be divided into three groups: orientation-dominated questionnaires, highly selective tests and multidomain tests. Multidomain tests are the most useful in aiding diagnosis (Brown, 2015). So far, over 40 brief cognitive tests have been developed and tested to identify people with cognitive impairment (Ozer, Young, Champ, & Burke, 2016).

The Mini-Mental State Examination (MMSE) has been the standard short cognitive test for more than 40 years (Folstein et al., 1975). It is a widely used psychometric test to screen for cognitive impairment as well as to track development of cognitive function over time (Molloy & Standish, 1997). This test evaluates a broad range of cognitive functions including orientation, recall, attention, calculation, language processing and constructional praxis. The MMSE has been demonstrated in many studies as valid and brief test that provides satisfactory screening of cognitive deficits and determines their severity at the time of evaluation (Mitchell, 2009; Tsoi, Chan, Hirai, Wong, & Kwok, 2015).

However, the MMSE has some disadvantages, including insensitivity to the earliest changes in highly educated individuals (O'Bryant et al., 2008) and a lack of ability to measure frontal/executive function. Another test designed to detect AD is Test Your Memory (TYM) introduced by Brown et al. (2009). The TYM, as a supervised, self-completed questionnaire comprising ten cognitive tasks is reported to be a valid and reliable screening test for the detection of AD. This test is quick to use, tests various skills, and takes minimal operator time to administer (Ozer, Noonan, et al., 2016).

The MMSE and TYM tests serve as measuring tools of progression or improvement of cognition in cognitive disorders (Mitchell, 2009; Tsoi et al., 2015). The MMSE test was originally made in English and were translated and scientifically validated in other languages such as Arabic (Abd-Al-Atty, Abou-Hashem, Abd Elaziz, Abd El Gawad, & El-Gazzar, 2012), Germanic (Milian et al., 2012), Spanish (Steis & Schrauf, 2009), Tiwanian (Liu et al., 1994), Czech (Bartos & Raisova, 2016) and Chinese (Tsai et al., 2015) languages. Also the TYM test is currently being translated into several different languages such as Japanese (Hanyu et al., 2011), Spanish (Ferrero-Arias & Turrion-Rojo, 2016), Hungarian (Kolozsvári et al., 2017), Turkish (Maviş et al., 2015), French (Postel-Vinay et al., 2014), Polish (Szczesniak, Wojtynska, & Rymaszewska, 2013) and Chinese (Li et al., 2018) languages.

The aim of the present study was to evaluate the effectiveness of the adapted MMSE and TYM tests for identifying elderly Iranian population with AD. We also determined the sensitivity and specificity for different cut-offs of the MMSE and TYM tests in predicting the clinical diagnosis of dementia.

Methods

Subject selection

All participants were recruited between May 2017 and February 2018. They passed a physical examination and completed forms of the MMSE and TYM tests. Participants with AD (AD group) enrolled in this study were the patients (65–90 years old) residing at the Welfare Organizations including Emam Ali (A private center in Tehran, Capital of Iran), and Golabchi (Kashan, Iran), Barekat (Aran-Bidgol, Iran) and Miad (Ravand, Iran), the 3 cities located in the center of Iran. All Welfare Organizations offer cares for aged people long life. Informed consent was obtained for experimentation from all participants. The diagnosis of AD was based on the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (McKhann et al., 1984). The history of care health records of the patients was screened and the participants who met the criteria for AD with a stable clinical condition and complete clinical evaluation were considered eligible for this study. The other inclusion criteria were absence of subjective cognitive complaints and no history of major head trauma.

The normal control group (CON group) consisted of elderly subjects were also examined by the specialist to confirm they are without any history or symptoms of neurologic or psychiatric diseases. Controls were recruited from random selection of elderly people in mosques, parks, the relatives of the students and the nurses in the health care centers.

The total sample comprised 174 participants distributed between the two groups: the AD group with 60 patients and the CON group with 114 cognitively healthy people. This research was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). Also the study was approved ethically by Ethical Committee of Kashan University of Medical Sciences. The participants were only introduced to the two cognitive tests and, hence, no intervention was performed. Figure 1 explains flow of AD and CON subjects selection enrolled in the study.

The MMSE and TYM tests

The original MMSE comprises 5 tasks (and scores) including orientation (10 scores), registration (3 scores), attention and calculation (5 scores), recall (3 scores) and language (9 scores). The total score is 30. The TYM includes a series of

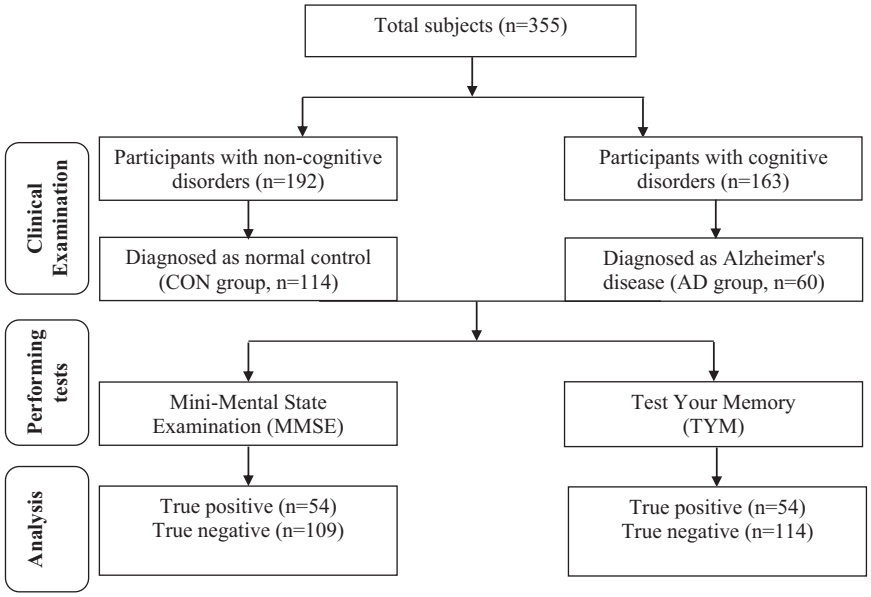

Figure 1. Summary of patient flow.

10 tasks (and scores) consists of: orientation (10 scores), ability to copy a sentence (2 scores), semantic knowledge (3 scores), calculation (4 scores), verbal fluency (4 scores), similarities (4 scores), naming (5 scores), visuospatial abilities (7 scores) and recall of a copied sentence (6 scores). The ability to do the test is also scored (5 scores) giving a possible total of 50 scores.

The adapted versions of MMSE and TYM

Minor modifications were applied to some questions in the MMSE and TYM tests based on a translation of the original English-language version into Farsi (Iranian language). In the fifth question of the MMSE test the word 'world' was substituted by 'rainy'; because it is difficult to pronounce two consecutive consonant letters in Farsi language. The two questions in the semantic knowledge section of the TYM were substituted by questions familiar to Iranian people. In the first question the subjects were asked to name the Iranian president rather than the UK prime minister. Also the second question of semantic knowledge 'In what year did the 1st World War start?' uncommon knowledge in Iran, was changed to 'In what year did the war between Iran and Iraq?'. The war was occurred between 1980 and 1988. Also we replaced the letter 'W' in the original version of TYM with the letter 'د' in Farsi alphabet. Trained research assistants who were blinded to each other's assessments administered the MMSE and TYM tests.

Validity of sensitivity and specificity of the tests

The area under curve (AUC) was reported based on receiver operating characteristic (ROC) analysis. The test cut-offs were determined empirically by examining optimal combination of sensitivity and specificity at all cut-off values with the optimal cut-off being defined by maximal test accuracy for diagnosis. Positive (PPV) and negative predictive values (NPV) with 95% confidence intervals were assessed at each of the cut-off point levels.

Data analysis

Since data were normally distributed, the comparisons between the AD and CON groups and between the males and females were made using unpaired t-test. Difference in gender proportion between the two groups was analyzed using the X^2 test. Pearson's correlation coefficient analysis was applied to evaluate probable correlation between the test scores with age. ROC curve analysis was applied to assess the ability of the MMSE and TYM global and subtest scores to discriminate between the AD and CON groups for a range of cut-off values. The analyses assumed an alpha risk of 0.05 in a bilateral contrast. Estimates are provided with their 95% confidence intervals. Statistical analyses were carried out using SPSS 16, Excel 2016 and Instat3. Descriptive statistics were presented as means ± standard error (SEM).

Results

Demographic data

The age of the participants ranged between 55 and 98 years; between 65 and 81 years in the CON subjects, and between 55 and 98 years in the patients with AD. The AD participants were significantly older than the CON people where the mean age was 80.07 ± 0.62 and 68.24 ± 0.45 years in the AD and CON groups, respectively ($P < 0.0001$). In the CON group 66 (58%) and 48 (42%) people were men and women, respectively. The AD group contained 20 (33%) men and 40 (67%) women. Totally, the sample ($n = 174$) included more percentage of female (61.9%) than males (38.1%) ($P < 0.002$). Table 1 displays the baseline demographic characteristics.

Neuropsychological characteristics

Neuropsychological evaluations confirmed 60 (34.48%) people with AD. The remaining 114 (65.52%) people were designated as controls and formed the reference group for the subsequent analyses. The TYM score of the participants assigned as normal people was 44.32 ± 0.389. Score of the

Table 1. Demographic characteristics of the control (CON) and Alzheimer's disease (AD) groups.

	Age		Sex	
	Mean of age (years)	Range of age (years)	Male (No/%)	Female (No/%)
CON (114)	68.24 ± 0.45	65–81	66 (58%)	48 (42%)
AD (60)	80.07 ± 0.62	55–98	20 (33%)	40 (67%)
Total (174)	72.32 ± 0.68	55–98	86 (49.4%)	88 (50.6)

Table 2. Comparison of total Mini-Mental State Examination (MMSE) scores and subscores among the control (CON) and Alzheimer's disease (AD) groups.

MMSE test	CON group	AD group	Difference	P value	Cut-off	Sen	Spe	PPV	NPV	AUC
Orientation (10)	9.74 ± 0.051	3.25 ± 0.365	6.487 ± 0.368	0.0001	8.5	0.95	0.96	0.93	0.97	0.984
Registration (3)	2.87 ± 0. 034	1.85 ± 0.157	1.018 ± 0.161	0.0001	2.5	0.57	0.88	0.71	0.80	0.742
Attention and calculation (5)	2.19 ± 0.200	0.32 ± 0.129	1.876 ± 0.238	0.0001	0.5	0.88	0.63	0.56	0.91	0.768
Recall (3)	1.46 ± 0.085	0.55 ± 0.117	0.906 ± 0.144	0.0001	0.5	0.67	0.86	0.71	0.83	0.770
Language (9)	7.51 ± 0.128	5.02 ± 0.244	2.492 ± 0.250	0.0001	5.50	0.73	0.92	0.83	0.87	0.854
Total (30)	23.77 ± 0.327	10.88 ± 0.762	12.889 ± 0.829	0.0001	18.5	0.90	0.96	0.91	0.95	0.962

Note. Sen, sensitivity; Spe, specificity; PPV, positive predictive value; NPV, negative predictive value; AUC, area under curve.

people proposed to have AD was 14.37 ± 1.368. According the MMSE test the scores were 23.77 ± 0.327 and 10.88 ± 0.762 in the CON and AD patients, respectively.

The MMSE test

Sensitivities and specificities for diagnosis of AD with optimal cut-off scores for the MMSE test are shown in Table 2. All tasks showed a significant difference between the CON and AD subjects. According to the MMSE test the AUC was 0.962 and a score of 18.5 was determined as optimal cut-off to differentiate between the control people and AD patients. At this cut-off the sensitivity and specificity were 0.90 and 0.96, respectively. The PPV value was found as 0.91 that means 91% of AD patients diagnosed correctly. Also based on the NPV index 95% of normal people diagnosed correctly. Six out of 60 and 5 out of 114 were diagnosed incorrectly in the AD and control groups, respectively.

Regarding the MMSE sub-scores the 'orientation' index showed the highest concurrent sensitivity (0.95) and specificity (0.96) as well as a maximum AUC (0.984). Therefore, considering the 'orientation' index the MMSE test resembles the TYM test. It should be pointed out that this index includes the same questions and sub-scores in both TYM and MMSE cognitive tests. Also the 'language' gained the second order in AUC (0.854). On the other hand, the 'registration' index displayed the lowest concurrent sensitivity (0.57) and specificity (0.88) with an AUC of 0.742. The 'recall' subtest (AUC = 0.770) also showed to be a weak index for assessment.

The TYM test

Sensitivities and specificities for diagnosis of AD with optimal cut-off scores, and PPV and NPV for the TYM test are shown in Table 3. All tasks showed a significant difference between the CON and AD subjects. The AUC was 0.991 based on the TYM cognitive test, and a score of 31 provided the optimal cut-off for discriminating between the CON and AD participants. At this cut-off the sensitivity and specificity were 0.9 and 1, respectively. In this test the PPV was 1 indicating that, according to TYM test, all AD patients diagnosed correctly. Some (6 out of 60) of the participants who assigned as AD people were scored as normal. On the other hand, the NPV index showed a value of 0.95 indicating that 95% of normal people diagnosed correctly.

Considering the TYM sub-scores the 'orientation' index was found to have the highest concurrent sensitivity (0.95) and specificity (0.96) with an AUC of 0.984. Also the 'anterograde' (AUC = 0.951) and 'semantic knowledge' (AUC = 0.949) displayed high sensitivity and specificity. On the other hand, the 'similarities' index showed the lowest concurrent sensitivity (0.67) and specificity (0.88) with an AUC of 0.798. The other weak indices were 'fluency' (AUC = 0.891), 'calculation' (AUC = 0.890) and 'copying' (AUC = 0.863).

Comparison of the MMSE and TYM results

Sensitivity and specificity of the MMSE and TYM tests compared to clinical diagnosis of dementia (NINCDS-ADRDA criteria) are presented in the Table 4.

The ROC curves (Figure 2) illustrate combined scores to compare the ability of the MMSE and TYM tests for distinguishing the normal people and those with Alzheimer's disease. The ROC analysis demonstrated that the AUC was 0.991 and 0.962 measured by the TYM and MMSE tests, respectively. Whereas the MMSE test indicated a gap of about 13 scores between the CON and AD subjects, the TYM score gap was about 30 between the two groups. It means that the gap percentage was 43.3% and 60%in the MMSE and TYM tests, respectively.

The difference between the CON and AD subjects based on the MMSE and TYM cognitive tests is shown in Figure 3a and b, respectively. In the MMSE test there is a clear separation of most individuals; only the normal people scored $\geq$23 and only the patients with AD scored $\leq$9. On the other hand, performance of the TYM test made a further separation between the CON and AD groups where the former scored $\geq$43 and the latter scored $\leq$10.

Relevancy of the test scores with age

We assessed probable correlation between the scores of both tests with age. Pearson's analysis indicated no correlation between age with the MMSE and TYM scores in the CON group. Concerning the AD group, a positive Pearson's correlation coefficient was evident between age and the

Table 3. Comparison of total Test Your Memory (TYM) scores and subscores among the control (CON) and Alzheimer's disease (AD) groups.

TYM test	CON group	AD group	Difference	P value	Cutoff	Sen	Spe	PPV	NPV	AUC
Orientation (10)	9.74 ± 0.051	3.25 ± 0.365	6.487 ± 0.368	0.0001	8.5	0.95	0.96	0.93	0.97	0.984
Copying (2)	1.75 ± 0.044	0.52 ± 0.102	1.238 ± 0.111	0.0001	0.50	0.67	0.98	0.95	0.85	0.863
Semantic knowledge (3)	2.41 ± 0.074	0.30 ± 0.096	2.112 ± 0.121	0.0001	0.50	0.82	1	1	0.91	0.949
Calculation (4)	3.18 ± 0.116	0.77 ± 0.151	2.409 ± 0.194	0.0001	2.50	0.90	0.76	0.67	0.93	0.890
Fluency (4)	3.73 ± 0.074	0.95 ± 0.189	2.778 ± 0.203	0.0001	2.50	0.81	0.96	0.92	0.91	0.891
Similarities (4)	3.75 ± 0.070	1.77 ± 0.232	1.979 ± 0.243	0.0001	3.50	0.67	0.88	0.75	0.83	0.798
Naming (5)	4.91 ± 0.049	1.92 ± 0.248	2.996 ± 0.253	0.0001	4.50	0.82	0.96	0.91	0.91	0.897
Visuospatial 1 (3)	2.77 ± 0.058	0.48 ± 0.133	2.289 ± 0.146	0.0001	1.50	0.83	0.95	0.89	0.91	0.916
Visuospatial 2 (4)	3.91 ± 0.036	1.08 ± 0.188	2.829 ± 0.191	0.0001	3.50	0.88	0.95	0.90	0.95	0.933
Anterograde (6)	3.71 ± 0.140	0.50 ± 0.118	3.211 ± 0.183	0.0001	1.50	0.87	0.92	0.85	0.93	0.951
Executive (help) (5)	4.49 ± 0.083	2.92 ± 0.064	1.575 ± 0.105	0.0001	3.50	0.95	0.84	0.76	0.97	0.904
Total (50)	44.32 ± 0.389	14.37 ± 1.368	29.949 ± 1.422	0.0001	31	0.90	1	1	0.95	0.991

Note. Sen, sensitivity; Spe, specificity; PPV, positive predictive value; NPV, negative predictive value; AUC, area under curve.

Table 4. Comparison of sensitivity and specificity of the Mini-Mental State Examination (MMSE) and Test Your Memory (TYM) tests between the control (CON) and Alzheimer's disease (AD) participants.

		Gold state (NINCDS-ADRDA criteria for diagnosis of AD)									
Test		Positive	Negative	Cut-off	Sen	Spe	PPV	NPV	AUC	CCR	P Value
TYM	**Positive**	54	0	31	0.90	1	1	0.95	0.991	96.5	0.0001
	Negative	6	114								
MMSE	**Positive**	54	5	18.5	0.90	0.96	0.91	0.95	0.962	93.6	0.0001

Note. Sen, sensitivity; Spe, specificity; PPV, positive predictive value; NPV, negative predictive value; AUC, area under curve; CCR, correct classification rate.

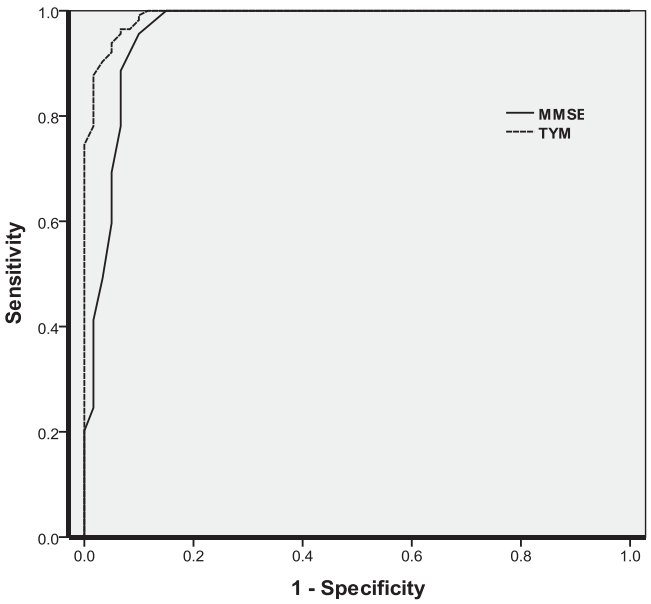

Figure 2. Receiver operating characteristic (ROC) curves screening for Alzheimer's disease. The curves show the relationship between probability of a hit (true positive) and a false alarm (false positive) for the Mini-Mental State Examination (MMSE) and Test Your Memory (TYM) scales in the healthy controls (CON group, n = 114) and the patients with Alzheimer's disease (AD group, n = 60).

MMSE ($R = 0.42$, $P \leq 0.001$) and TYM ($R = 0.492$, $P \leq 0.001$) scores.

Sex dependency of the test scores

To evaluate if how the males and females respond the cognitive tests the scores achieved by the two groups were also analyzed by t-test. The statistical analysis indicated that, in the two groups, the females outperformed the males in both MMSE and TYM tests ($P \leq 0.001$). The MMSE scores attained by the CON males and females were 22.24 ± 0.407 and 25.88 ± 0.383, respectively. In AD patients the values were 5.45 ± 0.569 and 13.6 ± 0.819 in the males and females, respectively. Also, in the TYM test the CON males and females scored 41.88 ± 0.47 and 47.67 ± 0.172, respectively. In the AD patients the males and females achieved scores of 4.45 ± 0.285 and 19.33 ± 1.529, respectively.

Discussion

Using the adapted versions of two widespread cognitive tests MMSE and TYM we attempted to determine the ability of each of them in both diagnosis of AD and making separation between cognitive characteristics of the normal and AD people. Analyzing data reflected in the AUC screening curves (Figure 2) and distribution of scores (Figure 3) indicated that both cognitive tests are confident to apply on the elderly population in several areas of Iran. The scores in the original version of the MMSE test are: 27–30, as normal; 21–26 as mild, 11–20 as moderate and 0-10 as severe. However, the most widely used cut-off to suggest dementia is score of 24 (Albanna et al., 2017). The cut-off score obtained in our study for diagnosis of AD was 18.5.

Although the MMSE test assesses several different cognitive domains and especially is useful for evaluation of orientation, however, it includes only a single point for visuospatial tasks and is ease to its memory, language, and visuospatial tasks (Galasko et al., 1990; O'Bryant et al., 2008). These disadvantages lead to the main problem in that it is insensitive in the diagnosis of mild AD (Galasko et al., 1990; Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000; O'Bryant et al., 2008; Tombaugh & McIntyre, 1992). Brown et al believe that despite much strength the MMSE test is only valuable in the assessment of patients with recognized dementia, and, it fails testing a wide range of cognitive tasks and sensitivity to mild AD (Brown et al., 2009). Furthermore, previous studies indicate that MMSE scores may be influenced by age, education level, cultural background, social class, literacy and language (Freidl et al.,

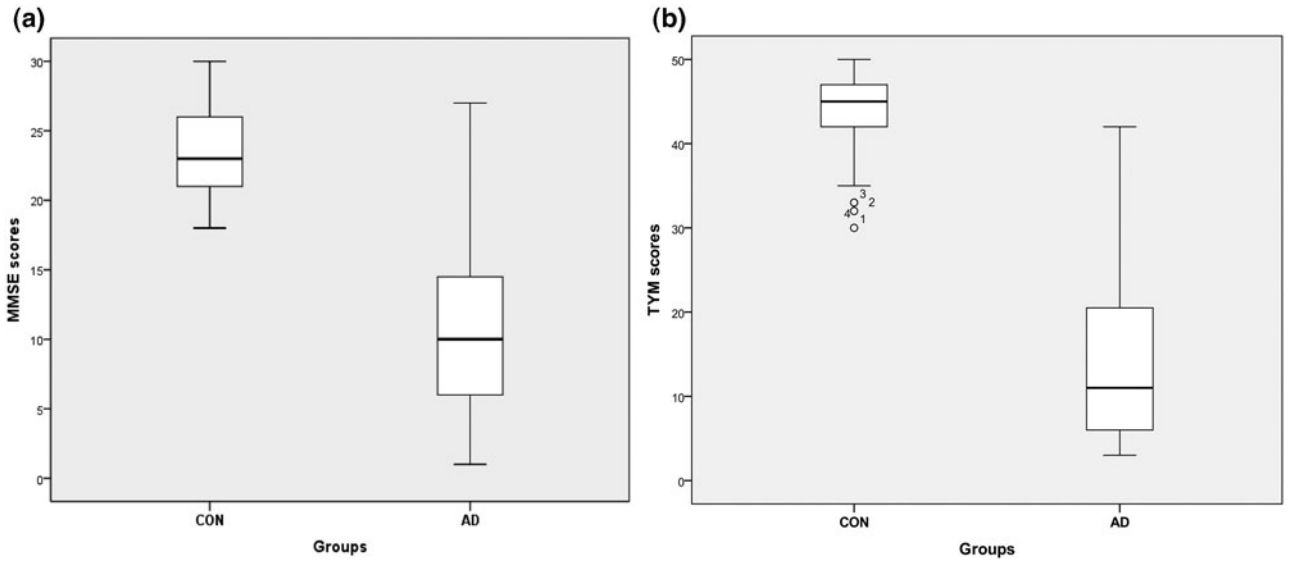

Figure 3. Box plot showing the distribution of (a) the Mini-Mental State Examination (MMSE) and (b) Test Your Memory (TYM) scores among the control (CON) and Alzheimer's disease (AD) groups.

1996; Jorm, Scott, Henderson, & Kay, 1988; Liu et al., 1994; Lopez, Charter, Mostafavi, Nibut, & Smith, 2005). In the Japanese version of MMSE Sakuma et al. gained an average score of 28 in most of people with average education level of 12.6 ± 2.9 years (Sakuma et al., 2017). In Czech version of MMSE gained an average score of 28 ± 2 in the people with average education level of 14 ± 3 years (Bartos & Raisova, 2016). Since the people enrolled in our study were either uneducated or with a very low education, therefore, the cut-off score of 18.5 for diagnosis of AD in our study can be expectable.

On the other hand, the TYM is psychometrically robust and broad in its coverage of cognitive domains, leading to less bias. This cognitive test is a supervised, self-completed questionnaire comprising cognitive tasks. In addition to memory and orientation tasks, the TYM also includes calculation, fluency, similarities, naming, and visuospatial tasks. Moreover, it is believed that the TYM is more sensitive than the MMSE in screening for non-Alzheimer's dementias (Brown et al., 2009). It is reported that although the TYM compares favorably with the MMSE as a screening test for cognitive impairment, however, the TYM display a higher internal consistency and easily self-administration (van Schalkwyk, Botha, & Seedat, 2012). This test has been used in several countries and in many translated versions with good results (Abd-Al-Atty et al., 2012; Hancock & Larner, 2011; Hanyu et al., 2011; Kolozsvári et al., 2017; Maviş et al., 2015; Ojeda, Salazar, Dueñas, & Failde, 2012). The scores introduced by developer of the TYM test are: 47–50, as normal; 33–47 as mild AD, 25–33 as moderate AD and <25 as severe AD. The cut-off for AD in our study was 31. As reported by the developers of TYM we found that TYM has a very high sensitivity and specificity for discriminating between people with and without mild AD (Brown et al., 2009).

Concerning education level, the AD people in our study (at 8th and 9th decade of life) were either illiterate or with a very low literacy that behaved the same in responding to the tests.

We found no correlation between the cognitive performances and age in the CON group but a positive correlation in the AD patients. These results could be expectable; comparable cognitive behavior in the younger normal people compared to different cognitive function in the older AD patients (Table 1). On the other hand, the test scores gained by both groups were sex dependent, with more scores attained by the females. In two recently clinical published papers we also found that the TYM and MMSE tests are sensitive to age (Agahi et al., 2018; Akbari et al., 2016). Evidence from other versions of TYM test also indicates that this test is not so powerful cognitive screening test in uneducated or lower level educated individuals (Ferrero-Arias & Turrion-Rojo, 2016). Using Chinese version of TYM Li et al. reported a correlation between years of education and scores of TYM test in MCI people but not AD or normal control groups (Li et al., 2018). French version of TYM showed no effect of educational level, sex, or mood but a significant effect of age (Postel-Vinay et al., 2014). In a study on Polish people Szczesniak et al. suggested that the age and the level of education of the respondents should be considered when using the TYM test (Szczesniak et al., 2013).

Strengths and limitations of the study

Here, we proved that both cognitive tests are reasonably applicable in Iran's society. However, this work had some limitations. First, both the MMSE and TYM performance may be influenced by educational level. We did not evaluate the effect of education. Second, the subjects with problems in reading or writing, impaired visual acuity and severe AD, are unable to complete the test.

Conclusion

Overall, in regard to correct classification rate (CCR), the TYM test seems to be more appropriate for cognitive screening in our study. However, considering an analogous AUC, both tests are comparable and have high sensitivity and specificity for discriminating between people with and without AD. Our results and findings by others indicate that the TYM test is a cognitive tool which may be superior to some other neuropsychological tests such as the MMSE

for diagnosis of the AD patients from the healthy people. Nevertheless, studies in different countries indicate that, based on the population, some demographic characteristics of the respondents must be considered when using the TYM test. Also, some domains need to be further investigated, including prospective validity and sensitivity to change, expediency for different populations, clinical settings and vulnerability to cultural and educational bias (Ferrero-Arias & Turrion-Rojo, 2016).

Taken together, it seems that there is no still a universally valid cognitive screening test and regarding the target population every clinic can use the best matching test. However, despite a discrepancy between the two tests considering the total scores and the number and kind of tasks, however, both tests include some common cognitive domains and both shows acceptable concurrent validity.

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Disclosure statement

The authors report no conflict of interest.

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