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Original articles

Validity of the italian telephone version of the mini-mental state examination in the elderly healthy population

Nicola VANACORE*, Antonella DE CAROLIS**, Micaela SEPE-MONTI**, Giuseppe BOMBOI**, Antonia STAZI*, Angelo BIANCHETTI*** and Franco GIUBILEI**

***National Centre of Epidemiology, National Institute of Health, Rome, Italy ; ****Department of Neurological Sciences, "La Sapienza" University, Rome, Italy ; *****Department of Medicine and Rehabilitation "S. Anna" Hospital, Brescia and Geriatric Group, Brescia, Italy

Abstract

The biggest challenge regarding cognitive prospective evaluations in the elderly is the identification of subjects that go on to develop cognitive impairment. In this study, we compared the Italian telephone version of the MMSE (Itel-MMSE) with both the MMSE and a battery of neuropsychological tests in a group of 107 healthy elderly subjects. The aim of the study was to identify a subset of subjects who, despite having an overall score within the normal range, performed poorly in the cognitive neuropsychological evaluation. The Itel-MMSE score showed a good internal consistency as well as a significant correlation with the MMSE score, age and education. A score of ≤ 21 on the Itel-MMSE was the score which reflected the highest degree of sensitivity in the neuropsychological tests. There was a statistically significant difference between subjects with an Itel-MMSE score of ≤ 21 and those with a score of 22 in age, education, Attentional Matrices and Copying Drawings. Despite some potential limitations, our results strongly suggest that the Itel-MMSE may be used as a screening test to identify healthy elderly subjects whose cognitive performance is poor.

Key words : MMSE ; telephone MMSE ; neuropsychological evaluation, aging ; cognitive impairment ; mild cognitive impairment.

Introduction

The biggest challenge regarding cognitive prospective evaluation in the elderly is the identification of subjects that subsequently develop mild cognitive impairment (MCI) or dementia (Xu G. *et al.* 2002 ; Busse A. *et al.* 2003 ; Lipton R. B. *et al.* 2003). Approximately 20% of elderly subjects "cognitively normal" at the common screening instruments such as Mini Mental State Examination (MMSE) and Cambridge Cognitive Examination show a neuropsychological performance below the normal range (4). Such instruments have a number of limitations in wide population-base studies because of difficulties encountered in administering them to the whole population. In this regard, numerous telephone screening tests have been proposed to evaluate pathological cognitive status, and in particular Alzheimer's disease (AD), MCI and post-stroke dementia (5, 6, 7, 8). The most widely used telephone screening tests (TICS and TELE) have many elements in common with the MMSE, and they have high sensitivity and specificity in the differentiation of AD patients from healthy controls (9, 10). No data are, however, available regarding healthy elderly subjects. An Italian telephone version of the MMSE (Itel-MMSE) has recently been validated in a group of patients affected by dementia with varying degrees of the cognitive impairment (11). However, the Itel-MMSE was not validated to identify subjects with a poor cognitive performance in neuropsychological tests, although within normal range score.

In this study, we compared the Itel-MMSE with both the MMSE and a battery of neuropsychological tests in a group of healthy elderly subjects. The aim of our study was to identify a subset of subjects who, despite having an overall score within the normal range score, performed poorly in the cognitive neuropsychological evaluation. These subjects should be included in a prospective evaluation of cognitive status because they could have a high risk of developing MCI or dementia.

Methods and materials

A project is currently being conducted to identify, using the National Twin Registry, any cases of twins affected by cognitive deficit who are residents in the Rome area (12). A random sample of 321 (126 male and 195 female ; age 63.7 ± 1.1 years ; education 10.5 ± 4.4 years ; Itel-MMSE score 21.3 ± 1.3) healthy twins were identified in this project and the Itel-MMSE administered.

One hundred and fifteen of these 321 twins agreed to undergo a neuropsychological evaluation in our hospital outpatient memory clinic from January 2002 to May 2003. Eight twins (2 male and 6 female ; age 63.7 ± 1.6 years, education 9.5

Table 1

Cognitive items used on the Itel-MMSE

Item	Points
Date, month, year, day of week, season	5*
City, province, district, country	4*
Repeating "house, bread, dog"	3*
Counting backwards from 100 by sevens	5*
Recalling the 3 words (house, bread, dog)	3*
What do you call the object you are using to speak with me ? (telephone)	1
Say this "Tiger against tiger"	1
Total score	22

* one point given for correct answer to each part of question.

± 4.4 years) were excluded because of cognitive impairment found at the neuropsychological evaluation.

The Itel-MMSE score was 19.8 ± 1.6.

One hundred and seven healthy twins were, therefore, included in the study (34 male and 73 female ; age, 64 ± 1.6 years ; education, 10.6 ± 4.3 years). There was no statistical difference in the Itel-MMSE score, sex, age and years of education between the subjects included (n = 107) and those not included (n = 214) in our study.

The time interval between administration of the Itel-MMSE and the neuropsychological evaluation was less than one month. The Itel-MMSE is composed of seven items which assess the following cognitive domains : orientation, language comprehension and expression, attention and memory. The score range is 0 to 22 (Table 1).

The neuropsychological evaluation included the MMSE (13) and the following tests : Raven's Coloured Progressive Matrices (14), Story Recall (15), Verbal Fluency on Phonological cue (F-P-L) and Verbal Fluency on Semantic cue (animals) (16), Copying Drawings (17) and Attentional Matrices (18) for the evaluation of the following domains : general intelligence, episodic long-term memory, language abilities, visuo-spatial skills and selective attention. According to the distribution of Italian normative data, the raw score of each test was adjusted for age and education, and subdivided into five categories (from 0 to 4) with an ordinal relationship (equivalent score) (15, 16, 18, 19). In particular, zero indicated a performance corresponding to the worst 5% of the sample healthy population, while 4 indicated a score which was above the median value of the normal sample. The equivalent scores of 1, 2, and 3 were intermediate between 0 and 4 by equal interval of distribution values, according to the percentile partition of the left half of a normal distribution (20). Lastly, we considered the equivalent scores of 1-2 as a poor cognitive performance and the scores of 3-4 as a good one. The score of zero was considered as pathological.

Information related smoking, alcohol, hypertension, diabetes, dyslipidemia, cardiovascular disease was also collected. Informed consent for neuropsychological evaluation was obtained from all the participants.

Statistical analysis was performed by means of Pearson's correlation and Cronbach's alpha. Comparison between means was performed by Student's t test and Mann-Whitney test. Statistical analysis of the difference in the frequency of the categorical variables was performed by χ^2 test and odds ratio (OR) with a relative 95% confidence interval. A cut-off value of the Itel-MMSE predictive of a poor cognitive performance with a high sensitivity and specificity was identified. The equivalent score of 1-2 on neuropsychological tests was considered as "gold standard". All the analyses were performed using the SPSS statistical package (SPSS version 11).

Results

The Itel-MMSE, the MMSE and the neuropsychological scores are shown in Table 2. The result of the neuropsychological evaluation was normal in all the subjects, but 77 of the 107 subjects (72%) had a poor cognitive performance (equivalent scores of 1-2) in at least one neuropsychological test and 23 (21.5%) in at least two neuropsychological tests. The Itel-MMSE scores showed a good internal consistency (Cronbach's alpha = 0.37, p = 0.0007) and were significantly correlated with the MMSE scores (r = 0.262, p = 0.006), age (r = 0.203, p = 0.04) and education (r = 0.289, p = 0.002). There was, instead, no difference between males and females in the Itel-MMSE scores.

Two neuropsychological tests show a statistically significant correlation with the Itel-MMSE (Attentional Matrices r = 0.544, p = 0.001 and Copying Drawings r = 0.243, p = 0.012) and three one with MMSE (Phonological Fluency r = 0.331, p = 0.001 ; Semantic Fluency r = 0.334, p = 0.001 ; Story Recall r = 0.324 p = 0.001).

The estimate sensitivity and specificity of the Itel-MMSE scores are shown in Table 3. A score of $\leq$ 21 in the Itel-MMSE was the score which reflected the highest degree of sensitivity in the neuropsychological tests : Copying Drawings (67%), Attentional Matrices (75%), Phonological Fluency (35%), Semantic Fluency (23%), Raven's Coloured Progressive Matrices (41%), Story Recall test (47%). There was a statistically significant difference between subjects with an Itel-MMSE score of $\leq$ 21 (40 subjects) and those with a score of 22 (67 subjects) in age (63.6 ± 1.5 vs 64.3 ± 1.6 ; P = 0.04, Student's t-test), education (9.6 ± 4.7 vs 11.4 ± 3.8 ; P = 0.04), Attentional Matrices (51.4 ± 10.7 vs 62 ± 9 ; P = 0.001) and Copying Drawings (12.3 ± 1.2 vs 12.8 ± 0.9 ; P = 0.03). By contrast, no statistical difference was found between these two

Table 2

Itel-MMSE, MMSE and neuropsychological scores in 107 healthy elderly subjects

Test	Mean ± SD	Range	Normative value
MMSE	29.4 ± 0.9	25 - 30	≥ 24
Itel-MMSE	21.3 ± 1.0	18 - 22	–
Raven's Coloured Progressive Matrices*	28.4 ± 4.6	18.5 - 37.5	> 17.5
Phonological Fluency*	34.1 ± 8.6	17 - 59	> 16
Semantic Fluency*	19.4 ± 3.4	12 - 29	> 9
Attentional Matrices*	58.1 ± 10.9	32.2 - 76	> 30
Copying Drawings*	12.6 ± 1.1	8.2 - 14.2	> 7.75
Story Recall*	13.9 ± 3.6	8 - 24.5	> 7.5

* adjusted for age and education.

Table 3

Sensitivity and specificity of the Itel-MMSE scores in 107 healthy elderly subjects respect to neuropsychological tests (gold standard)

Neuropsychological test	Itel-MMSE					
	≤ 19 score		≤ 20 score		≤ 21 score	
	Sensitivity %	Specificity %	Sensitivity %	Specificity %	Sensitivity %	Specificity %
Copying Drawings	22	92	33	83	67	65
Attentional Matrices	25	93	58	86	75	67
Semantic Fluency	0	89	8	80	23	61
Phonological Fluency	13	92	17	81	35	62
Raven's Coloured Progressive Matrices	11	92	23	86	41	76
Story Recall	18	96	26	85	47	68

subgroups either in Story Recall, Raven's Progressive Matrices, Phonological and Semantic Verbal Fluency, or in sex, risk factors (smoking, alcohol, dyslipidemia) and diseases (OR = 0.80, CI 95%, 0.34-1.89 for hypertension ; OR = 1.77, CI 95%, 0.34-9.32 for diabetes ; OR = 1.67, CI 95%, 0.58- 4.86 for cardiovascular disease).

Discussion

The results of the present study suggest that the Itel-MMSE version may be used to identify healthy elderly subjects whose cognitive performance is poor. In particular, the Itel-MMSE score of ≤ 21 proved to have the best sensitivity in the identification of poor cognitive performance within the normal range. This degree of sensitivity was greater for Copying Drawings and Attentional Matrices than for Raven's Progressive Matrices, Story Recall, Phonological and Semantic Fluency. In this regard, an highly sensitive test is preferable to highly specific one in the screening phase as the sensitivity of a test is indicative of its ability to identify negative-false subjects, which may then be assessed more thoroughly in a subsequent phase by means of more accurate instruments.

The MMSE is difficult to use in wide population-base studies because its administration requests the presence of the subjects. Furthermore, the MMSE has been criticized both because of its low specificity in low educated subjects and because of its low sensitivity in the early phases of cognitive deficit associated with dementia (21, 22, 23). Nevertheless, a recent factor analysis provided evidence of the validity of this test for the assessment of cognitive status in the general population (24). Our results lend support to this finding. We, in fact, found that the Itel-MMSE administered to our elderly healthy subjects showed a good internal consistency and its results correlated with the MMSE.

The identification of subjects with a high risk of developing dementia or MCI is crucial for both the treatment of these patients and the epidemiological studies on cognitive decline. Four main advantages may be identified (25, 26, 27, 28, 29, 30) : a) to improve MCI epidemiological data, particularly those on incidence, prevalence, and conversion rate to dementia ; b) to investigate the interactions between genetic and environmental factors that may influence the cognitive decline ; c) to improve the design of clinical trials in MCI subjects ; d) to control both the diseases and the risk factors associated with MCI onset. Methodological factors are crucial in each of the above goals. In particular, guidelines are needed to select validated

neuropsychological tests designed to assess the cognitive decline in the screening phase (31). The first phase of any epidemiological study requires a good screening test. In this regard, some telephone tests have been validated to differentiate normal subjects from both MCI and dementia subjects, but there is not, to our knowledge, a validated test that identifies normal subjects with a poor cognitive performance. As such subjects may hypothetically be at risk of developing MCI and/or dementia, they should be included in a prospective cognitive evaluation. We have thus planned a longitudinal study to follow the cognitive performances of these subjects over the years.

In conclusion, despite the potential limitation due to the limited age range of the enrolled subjects and the weak correlation between MMSE and Itel-MMSE, our results suggest that the Itel-MMSE may be used as screening test to identify healthy elderly subjects with a poor cognitive performance. Further investigations are warranted to evaluate the ability of the Itel-MMSE to identify subjects over 65 year of age whose cognitive performance is poor, as well as to shed light on the cognitive changes which occur in healthy elderly subjects.

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Prof. F. GIUBILEI,
Clinica Neurologica,
Ospedale Sant'Andrea,
Via di Grottarossa 1035-1039,
00189 Rome (Italy).
E-mail : franco.giubilei@uniroma1.it.