

Feasibility of a Multiple-Choice Mini Mental State Examination for Chronically Critically Ill Patients

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Objectives: Following treatment in an ICU, up to 70% of chronically critically ill patients present neurocognitive impairment that can have negative effects on their quality of life, daily activities, and return to work. The Mini Mental State Examination is a simple, widely used tool for neurocognitive assessment. Although of interest when evaluating ICU patients, the current version is restricted to patients who are able to speak. This study aimed to evaluate the feasibility of a visual, multiple-choice Mini Mental State Examination for ICU patients who are unable to speak.

Design: The multiple-choice Mini Mental State Examination and the standard Mini Mental State Examination were compared across three different speaking populations. The interrater and intrarater reliabilities of the multiple-choice Mini Mental State Examination were tested on both intubated and tracheostomized ICU patients.

Setting: Mixed 36-bed ICU and neuropsychology department in a university hospital.

Subjects: Twenty-six healthy volunteers, 20 neurological patients, 46 ICU patients able to speak, and 30 intubated or tracheostomized ICU patients.

Interventions: None.

Measurements and Main Results: Multiple-choice Mini Mental State Examination results correlated satisfactorily with

standard Mini Mental State Examination results in all three speaking groups: healthy volunteers: intraclass correlation coefficient = 0.43 (95% CI, -0.18 to 0.62); neurology patients: 0.90 (95% CI, 0.82–0.95); and ICU patients able to speak: 0.86 (95% CI, 0.70–0.92). The interrater and intrarater reliabilities were good (0.95 [0.87–0.98] and 0.94 [0.31–0.99], respectively). In all populations, a Bland-Altman analysis showed systematically higher scores using the multiple-choice Mini Mental State Examination.

Conclusions: Administration of the multiple-choice Mini Mental State Examination to ICU patients was straightforward and produced exploitable results comparable to those of the standard Mini Mental State Examination. It should be of interest for the assessment and monitoring of the neurocognitive performance of chronically critically ill patients during and after their ICU stay. The multiple-choice Mini Mental State Examination tool's role in neurorehabilitation and its utility in monitoring neurocognitive functions in ICU should be assessed in future studies.

Key Words: cognition disorders; cognitive dysfunction; neurobehavioral changes in critical illness; neuropsychological tests; prolonged intensive care

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After their discharge from ICUs and hospital, chronically critically ill patients become associated with higher mortality rates and a poor quality of life (1). These patients are more prone to neurological dysfunction involving the CNS and peripheral nervous system. More specifically, neuropsychological and neurocognitive assessments show a persistent morbidity in ICU survivors (2). Manifestations of CNS failure include prolonged coma, chronic delirium and agitation, as well as neurocognitive and emotional sequelae (3).

Lasting neurological dysfunction has been underestimated and underreported in ICU populations and has only recently been studied (4). The prevalence of long-term neurocognitive impairment has been reported to be as high as 70% in acute respiratory distress syndrome survivors (5). Neurocognitive impairment was reported as early as 2 months following ICU treatment (6) and could last for up to 6 years (7). The etiology of neurocognitive impairment appears to be multifactorial

(8–11). Patients with preexisting cognitive impairment presented more neurocognitive impairment during and after their ICU stay (12). Severe sepsis was independently associated with enduring cognitive and functional limitations (13). Research has also shown that the development of delirium during ICU admission is one of the strongest predictors of prolonged neurocognitive impairment and mortality (14, 15). Approximately, a third of ICU survivors display serious chronic functional disabilities due to long-term neurocognitive or neuromuscular impairment (14).

Current ICU tools used for assessment are the Glasgow Coma Scale (GCS) (16) for the state of consciousness; the Sedation-Agitation Scale (SAS) (17); the Richmond Agitation Sedation Scale (18, 19) or the Ramsay score (20) for the degree of sedation or agitation; and the Confusion Assessment Method for ICU (21) for delirium. These scores are useful for assessing fluctuations of neurological status during the acute phase. However, these tools, used to assess sedation, agitation, and delirium in ICU, are unable to measure cognitive function or the aspects of cognitive function most applicable to cognitive recovery in the post-ICU period, such as executive function, visual-spatial recognition, memory-recall, problem solving, or reading.

The Mini Mental State Examination (MMSE) is a well-established, reliable, validated, and brief cognitive screening instrument (22). It is widely used in internal medicine, geriatrics, and neurology to assess the degree of cognitive impairment and to monitor cognitively impaired patients (23). The advantages of the MMSE are that the test is easy to administer and can be carried out by nonspecialists in clinical settings. It is divided into six items that are analyzed separately, that is, orientation, immediate recall, attention and calculation, delayed recall, language, and praxis (a three-stage command). Since accurate screening and early detection of neurocognitive impairments in ICU could positively influence early interventions, treatment, and planning of healthcare, we sought to assess whether a visual multiple-choice MMSE (MC-MMSE) could be used on chronically critically ill patients who are unable to speak.

MATERIALS AND METHODS

The visual version of the MMSE with multiple-choice responses (MC-MMSE) was elaborated internally by M.V. using the French Groupe de réflexion sur les évaluations cognitives (GRECO) version of the original questionnaire designed by Folstein et al (22); it was then checked by the study's neurologist (**Supplemental Digital Content 1**, <http://links.lww.com/CCM/A884>). We replaced “department” with “canton” for geographical specificity in Switzerland. Each spoken question had multiple-choice answers written on one page. The total questionnaire comprised 21 pages. The examiner asked the questions orally according to Folstein's protocol instructions and then presented the relevant page with the multiple-choice answers to the patient. The patient had to indicate the chosen answer with his finger or eyes, with the examiner indicating the response consecutively back to him. The sections of three-stage commands, writing a sentence and copying the complex polygon, were executed as in the original MMSE, the two latter with

the help of a steady support held in front of the patient and a thick board marker. Before starting the test, special precautions were taken to ensure a general level of comfort of the patient, such as their body position, wearing of glasses or hearing aids, and a quiet environment.

The two research assistants underwent MMSE administration training and their testing performances were evaluated and certified by the study's neurologist.

Four groups were deemed necessary to assess this test's usability and reliability: three speaking groups—healthy volunteers, neurology patients, and ICU patients able to speak—and a group of intubated or tracheostomized ICU patients.

The inclusion criteria for all four groups were as follows: being fully alert; a GCS higher than 12; a SAS between 3 and 5; being a fluent French speaker; over 18 years old; and with no hyper- or hypotension. Furthermore, healthy volunteers had to have been off any medication for the previous 24 hours, and the fourth group of ICU patients had to be either intubated or tracheostomized. For all four groups, refusal, end of life, and inability to write were exclusion criteria.

The MC-MMSE was compared with the standard MMSE (GRECO) in the three different groups whose participants could speak: healthy volunteers ($n = 26$); neurology patients ($n = 20$); and ICU patients able to speak ($n = 46$). The order of administration of the MC-MMSE and the standard MMSE was randomized. The two tests were administered 1–4 hours apart and were performed by the same examiner.

The interrater reliability of the MC-MMSE was determined by having this test administered twice to 20 intubated patients, once by each examiner. The order of the examiners was randomized, and the tests were administered 1–4 hours apart.

The intrarater reliability of the MC-MMSE was studied by the same examiner repeating the administration of the test twice to 10 intubated patients, 1–4 hours apart.

Consecutive ICU patients were prospectively included according to the inclusion criteria. The neurological patients were convenience samples in order to include a wide range of MMSE scores. The patients' demographic and anamnestic data, their diagnosis at admission, and data on their ICU stay and on any medication taken during the 24 hours prior to the test were collected (**Supplemental Digital Content 2**, <http://links.lww.com/CCM/A885>).

Ethical Issues

This study was approved by the Hospital Ethics Committee. Written informed consent was obtained from healthy volunteers, patients, or relatives when the patient was judged incompetent.

Statistical Considerations

Characteristics of subjects were expressed as mean \pm SD. The MMSE and MC-MMSE scores were expressed as a median and range and were compared using the sign test for paired data. A p value of less than 0.05 was considered statistically significant. To evaluate the agreement between MMSE and MC-MMSE scores, the mean difference (\pm SD) was assessed

and the Bland-Altman plots were reported with their limits of agreement (24). As the order of the examinations was randomized using a randomization program with sealed opaque envelopes, the potential impact of the order on the difference of scores was tested (Wilcoxon test). The intraclass correlation coefficient (ICC) was also assessed, using a method appropriate to nonnormal distributions (25). These analyses were conducted in healthy volunteers, neurology patients, and ICU patients able to speak. Interrater reliability was assessed in a similar way for 20 intubated patients, always using the same two examiners, but in a randomized order. The intrarater reliability was assessed in 10 intubated patients. All analyses were performed using Stata statistical software, release 11.0 (Stata, College Station, TX), Statview (SAS Institute, Cary, NC), and S-plus 8.0 for Windows (Insightful, Seattle, WA).

RESULTS

Between April 1, 2008, and September 1, 2009, 26 healthy volunteers, 20 patients in the Neurology department, and 76 ICU patients were enrolled in the study (Fig. 1).

Table 1 shows the demographic and clinical characteristics of the participants.

The median and range of the total and the 6-item scores of the standard MMSE and MC-MMSE are given in Table 2. The differences, both for the total scores and the 6-item scores, between the MC-MMSE and the MMSE together with the detailed limits of agreement in the three speaking groups (healthy volunteers, neurology patients, and ICU patients able to speak) are given in Table 3 and graphically in Figure 2. The limits of agreement for the three speaking groups were relatively good but showed a systematic bias toward a higher score for the results using MC-MMSE than for the results using standard MMSE. The ICU patients able to speak showed a greater bias in the delayed recall item, and the neurology patients showed a greater bias in the

orientation and delayed recall items. For the healthy volunteers, the mean MC-MMSE exceeded the standard version by less than one point, and the limits of agreement (i.e., where 95% of the difference is) ranged between around -2 and 3 points. For the neurology patients, the mean MC-MMSE exceeded the standard version by around one and a half points, and the limits of agreement ranged between around -3.5 and 7 points. The limits of agreement of the ICU patients able to speak were similar to those for neurology patients, and the mean MC-MMSE only exceeded the standard version by one point.

The ICC for the healthy volunteer group was 0.43 (95% CI, -0.18 to 0.62); for the neurology patients group it was 0.90 (0.82-0.95); and for the group of ICU patients able to speak it was 0.86 (0.70-0.92).

The order effect for the healthy volunteer group was slightly significant ($p = 0.048$), but no order effects were detected for the neurology patients group or the group of ICU patients able to speak ($p = 0.59$ and $p = 0.93$, respectively).

Even though individual differences between the two tests were fairly varied, as carried out, the analysis allowed the calculation of an acceptable mean difference between the two tests (limits of agreement). The analysis provided a way of converting standard MMSE scores to MC-MMSE scores and vice versa, but further research is needed to improve the precision of this conversion.

The ICC measuring inter- and intrarater reliabilities (Table 4) was around 0.95 despite the slight difference between examiners and examinations. Corresponding Bland-Altman plots are shown in Figure 3.

DISCUSSION

The standard MMSE designed by Folstein et al (22) cannot be administered to patients who are unable to speak, such as ICU patients with endotracheal tubes or tracheostomies. Thus, it seemed important to create a new tool that would fulfill two

aims: first, to be able to evaluate the cognitive functions of chronic critically ill patients, and second, to provide results that can be compared with more common tests in order to ensure continuity in the follow-up of such patients.

This study's major finding was that the new visual version of the MC-MMSE produced usable results with values close to those of the standard MMSE, independently of the population studied. Indeed, the global difference (bias) between both scores was only around one point higher for MC-MMSE, and the agreement analysis proved good for all types of

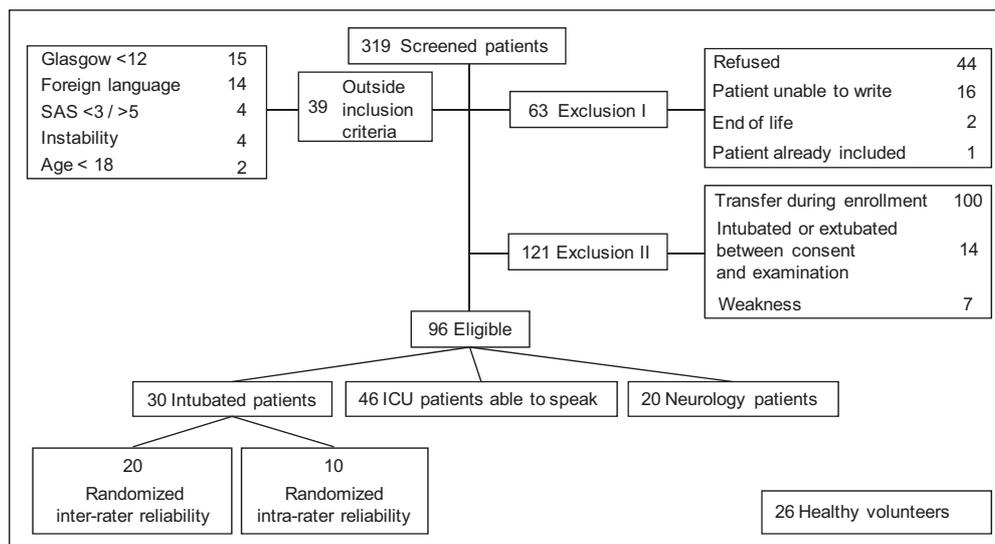


Figure 1. Consort. SAS = Sedation-Agitation Scale.

TABLE 1. Demographics and Clinical Characteristics of the Healthy Volunteers, Neurology Patients, and ICU Patients Able to Speak and Intubated Patients

Total: <i>n</i> = 122	Healthy Volunteers (<i>n</i> = 26)	Neurology Patients (<i>n</i> = 20)	ICU Patients Able to Speak (<i>n</i> = 46)	Intubated Patients (<i>n</i> = 30)
Demographic data				
Age, yr (mean ± sd)	43 ± 15	62 ± 14	62 ± 14	72 ± 16
Gender, male [<i>n</i> (%)]	11 (42)	9 (45)	36 (78)	19 (63)
Education, yr (mean ± sd)	19 ± 5	14 ± 5	14 ± 4	15 ± 6
Anamnesis data [<i>n</i> (%)]				
Smokers	–	2 (10)	16 (34)	12 (40)
Sedatives, opioids	–	0	0	2 (6)
Daily alcohol intake	–	2 (10)	8 (17)	8 (26)
Cognitive impairments: stroke, depression, dementia, and hydrocephaly	–	2 (10)	2 (4)	3 (10)
Diagnosis (<i>n</i> [%/total diagnosis (122)])				
Healthy	26 (21)	–	–	–
Respiratory failure	–	–	9 (7)	14 (11)
Cardiology and hemodynamic	–	–	16 (13)	4 (3)
Neurology	–	20 (16)	6 (5)	0
Cardiovascular surgery	–	–	5 (4)	2 (1.6)
Thoracic surgery	–	–	0	2 (1.6)
Visceral surgery	–	–	3 (2.5)	4 (3.2)
Other	–	–	7 (5.7)	4 (3.2)
ICU stay data				
Simplified Acute Physiology Score II (mean ± sd)	–	–	34 ± 14	48 ± 17
Mechanical ventilation, hr [median (range)]	–	–	–	154 (15–796)
Length of stay, d [median (range)]	–	–	4 (0.5–69)	27 (15–125)
Nine Equivalent of Nursing Manpower Score [median (range)]	–	–	21 (9–40)	27 (9–40)

Dashes indicate data not applicable.

participants studied, except for the healthy volunteers. In parallel, the poor correlation for the healthy volunteers group could be foreseen and can be explained by their very high scores.

The results of the interrater and intrarater reliability tests were also good, especially when taking into account the expected neuropsychological fluctuations of ICU patients. Analysis of intrarater reliability showed a slightly higher result in examination 2. The variability between the two examinations was quite important despite the few hours that separated them. However, these results were in line with a reference article that reported a great variability of the standard MMSE according to age and educational level (26). Since the order of the examinations was randomized and the order effects were moderate, a learning effect bias between the two tests could be excluded. Also, the most important differences in scores between the MC-MMSE and the standard MMSE were to be found in the delayed recall item for

neurological patients and ICU patients able to speak and the orientation item for neurological patients. The MC-MMSE seemed to be more difficult than the standard MMSE in the attention and calculation item, but easier in the recall and language items. Although the present study was not designed to analyze these differences, it is not surprising that showing written answers may have facilitated both the recall and language items. The poorer results in the attention and calculation items could be explained by the fact that, in the visual version, the patient not only had to do a mental calculation (as in the standard MMSE) but also had to pick out the correct number from a sheet containing other numbers, which could be confusing. This could prove even more difficult for ICU patients.

The new tool was easy to use at a critically ill patient's bedside, and even with such patients, the procedure only took 10–30 minutes to carry out. This information is important

TABLE 2. The Total and 6-Item Scores of Standard Mini Mental State Examination and Multiple-Choice Mini Mental State Examination in Healthy Volunteers, Neurology Patients, and ICU Patients Able to Speak

Scores	Healthy Volunteers			Neurology Patients			ICU Patients Able to Speak		
	MMSE	MC-MMSE	<i>p</i>	MMSE	MC-MMSE	<i>p</i>	MMSE	MC-MMSE	<i>p</i>
Total, median (range)	29 (27–30)	30 (27–30)	0.007	22 (6–29)	23.5 (11–29)	0.03	25 (12–29)	26 (12–30)	0.008
Orientation	10 (9–10)	10 (9–10)	1	8 (0–10)	8.5 (4–10)	0.07	9 (3–10)	9 (5–10)	1
Immediate recall	3 (3–3)	3 (3–3)	1	3 (1–3)	3 (1–3)	1	3 (0–3)	3 (1–3)	0.63
Attention and calculation	5 (3–5)	5 (3–5)	0.22	2.5 (0–5)	3 (0–5)	0.73	3 (0–5)	3 (0–5)	0.09
Delayed recall	3 (2–3)	3 (2–3)	0.13	2 (0–3)	2 (0–3)	0.12	2 (0–3)	3 (0–3)	< 0.0001
Language	8 (7–8)	8 (7–8)	0.03	7 (3–8)	7 (3–8)	0.75	7 (5–8)	7 (4–8)	0.09
Three-stage command	1 (1–1)	1 (1–1)	1	0.5 (0–1)	1 (0–1)	1	1 (0–1)	1 (0–1)	0.38

MMSE = Mini Mental State Examination, MC-MMSE = multiple-choice Mini Mental State Examination.

TABLE 3. Differences for the Total Scores and the 6-Item Scores Between Multiple-Choice Mini Mental State Examination and Mini Mental State Examination Together With Detailed Limits of Agreement (Bland-Altman) in the Three Speaking Groups (Healthy Volunteers, Neurology Patients, and ICU Patients Able to Speak)

Multiple-Choice Mini Mental State Examination–Mini Mental State Examination	Healthy Volunteers		Neurology Patients		ICU Patients Able to Speak	
	Mean (sd)	Limits of Agreement	Mean (sd)	Limits of Agreement	Mean (sd)	Limits of Agreement
Total	0.58 (1.17)	–1.72 to 2.87	1.50 (2.65)	–3.69 to 6.69	0.96 (2.21)	–3.38 to 5.29
Orientation	–0.04 (0.20)	–0.42 to 0.35	0.75 (1.41)	–2.01 to 3.51	0.07 (0.83)	–1.56 to 1.69
Immediate recall	0.00 (0.00)	0.00 to 0.00	–0.05 (0.51)	–1.05 to 0.95	–0.02 (0.39)	–0.79 to 0.75
Attention and calculation	0.19 (0.75)	–1.28 to 1.66	0.05 (0.94)	–1.80 to 1.90	–0.24 (1.08)	–2.35 to 1.88
Delayed recall	0.19 (0.49)	–0.77 to 1.16	0.55 (1.23)	–1.87 to 2.97	0.87 (1.09)	–1.26 to 3.00
Language	0.23 (0.43)	–0.61 to 1.07	0.15 (0.81)	–1.44 to 1.74	0.22 (0.92)	–1.58 to 2.01
Three-stage command	0.00 (0.00)	0.00 to 0.00	0.05 (0.51)	–0.95 to 1.05	0.07 (0.33)	–0.58 to 0.71

since ICU patients are often wrongly considered incompetent. Furthermore, this study showed that a majority of patients managed a score of 23 and more, which had been considered the cutoff for competence in previous studies (27–29). Many intubated patients, therefore, exhibited less cognitive impairment than caregivers previously thought. This is indeed important information since it could readily influence caregivers' general attitudes toward patients.

To our knowledge, this was the first attempt to adapt the standard MMSE to an ICU context in order to assess the neuropsychological state of chronically critically ill patients. Indeed, current tools, such as the GCS (16) or the U.S. National Institutes of Health stroke scale (30), were designed for acute care, but not for chronically critically ill patients. We considered several types of tests before designing the new tool. One

of the options was the Rancho Levels of Cognitive Functioning Scale. This is an eight-level rating scale of a patient's overall level of consciousness and his cognitive and behavioral functioning; it is commonly used to classify patients in acute and postacute rehabilitation settings (31). This option was rejected because the Rancho scale is indicated for use during the rehabilitation phase but is not recommended during the acute phase. Another tool considered for assessment purposes was the Mini-Cog Test (32). This is a rapid screening test for Alzheimer's disease that takes only 3–5 minutes to administer. Unlike the MMSE, which measures several aspects of cognition, the Mini-Cog measures only two dimensions: short-term recall and clock drawing. Such a test seemed too simple and not specific enough to enable detection and distinction of slight cognitive dysfunctions. Since ICU patients frequently suffer

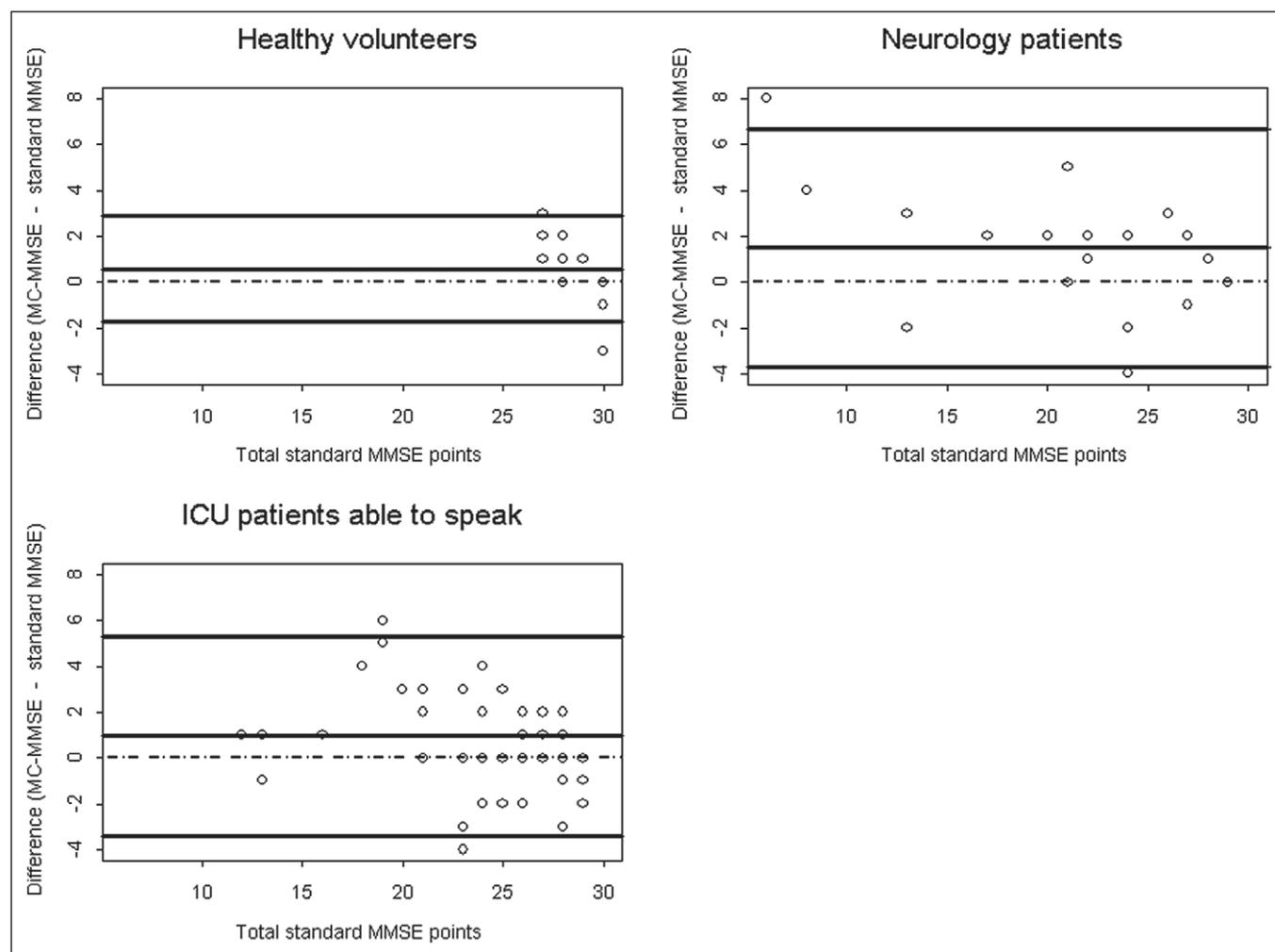


Figure 2. Differences for the total score and 6-item score between multiple-choice Mini Mental State Examination (MC-MMSE) and Mini Mental State Examination (MMSE) together with detailed limits of agreement (Bland-Altman) in the three speaking groups (Healthy volunteers, Neurology patients, and ICU patients able to speak).

from edemas and motor weaknesses, a first option consisting of an entirely written version of a test was abandoned. Although recent articles have suggested the superiority of the Montreal Cognitive Assessment over the MMSE for the determination of cognitive impairment in specific diseases (33), another recent broad ranging work reported that the MMSE is the instrument most extensively studied (34). The present study aimed not to determine the best test for critically ill patients but to allow a better follow-up of their cognitive function even after ICU discharge. As the MMSE is the most widely used instrument, including in our own institution, it seemed appropriate that this should be the tool tested.

Some qualitative findings seem worth reporting here. We found that the MC-MMSE was looked upon as an interesting mental exercise by the patients themselves; they both appreciated and felt stimulated by it. Some patients took the opportunity to enter into confidential discussions with the caregiver. Also, after the examination, they spoke of their feelings about this special experience. Another interesting finding was that some patients, considered to be confused

and completely perturbed, showed such good MMSE scores that their mental status had to be reconsidered. These results persuaded caregivers to modify their attitudes toward those patients whom they had previously tended to consider as incompetent.

Limitations

There are some limitations in this study. First, the sizes of the populations studied were small. However, since we did not compare the populations, each participant acted as his own control for the comparison of the two tests, and the small numbers are statistically acceptable. The high degree of concordance found between the two tests across the three populations tends to confirm that the number of participants included was sufficient.

Second, the healthy volunteers were younger than the ICU and the neurological patients. The results of the MMSE are known to vary according to age and level of education; thus, it might have been worthwhile comparing the two tests among older healthy people. However, the fact that the two

TABLE 4. Interrater and Intrarater Reliability

Interrater reliability (n = 20)	
Examiner 1, median (range)	21 (10–28)
Examiner 2, median (range)	19 (13–28)
Difference (examiner 1–2), mean (sd)	0.55 (1.70)
Limits of agreement	–2.78 to 3.88
ICC (95% CI)	0.95 (0.87–0.98)
<i>p</i>	0.23
Intrarater reliability (n = 10)	
Examination 1, median (range)	20.5 (17–29)
Examination 2, median (range)	22.5 (17–30)
Difference (examiner 1–2), mean (sd)	–0.90 (2.18)
Limits of agreement	–5.17 to 3.38
ICC (95% CI)	0.94 (0.31–0.99)
<i>p</i>	0.69

ICC = intraclass correlation coefficient.

tests produced very similar results in this normal population helps to confirm the reproducibility of these tests. The reproducibility in the lower ranges of the scores was tested in the neurological patients.

Third, we did not try to modify the written parts of the test, and the edemas and muscle weaknesses of the ICU patients

may have interfered with the results. The inability to write was one of the exclusion criteria; the tests were administered only to patients who were able to perform this exercise. Since the patient acted as his own control, and the two tests were performed at most 4 hours apart, there are few reasons to think that their muscle strength would have altered in between. Potential fatigue could have influenced the results, but the test order randomization prevented such bias. However, adapting the test for patients unable to write could also be an area for further research.

Fourth, the conversion of individual scores from the MC-MMSE developed in the present study to the standard MMSE should be treated with great caution because of its lack of precision, even if on average the correlation is almost unbiased. As the inclusion criteria were designed to prevent the occurrence of random responses, we did not include patients who would have had very low MMSE scores.

CONCLUSIONS

The visual MC-MMSE could be used for chronically critically ill patients who are unable to speak. It produced similar results to those obtained from the healthy volunteers and ICU patients who were tested with the original version of the standard MMSE. Thus, this new test may be an interesting tool for use in the clinical arena for following up on the neurocognitive evolution of chronically critically ill patients. Furthermore, it may enhance caregivers’ sensitivity toward neurocognitive dysfunctions that are often unknown and could help patients by giving them objective information on

the evolution of their condition. Finally, the assessment of patients’ cognitive states during their ICU stay may provide important information to relatives about the patient’s capacity to understand them and later help relatives to anticipate the social and/or medical support that patients need upon hospital discharge.

Confirmation of these results in larger, more diverse samples is warranted. This tool’s utility in detecting early neurocognitive dysfunction should be assessed further, as should possible neuro-rehabilitation strategies to ensure adequate long-term follow-up.

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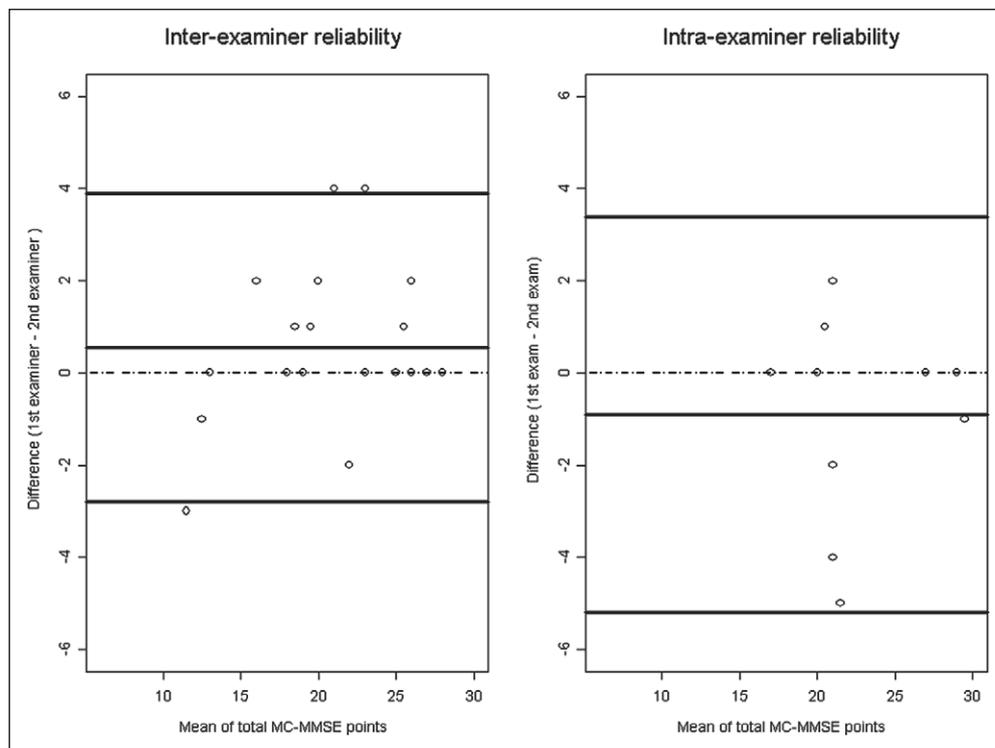


Figure 3. Inter- and intrareliability between multiple-choice Mini Mental State Examination (MC-MMSE) and standard Mini Mental State Examination (MMSE).

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