

THE MONTREAL COGNITIVE ASSESSMENT (MoCA) AS A MEASURE OF SEVERITY OF AMNESIA IN PATIENTS WITH ALCOHOL-RELATED COGNITIVE IMPAIRMENTS AND KORSAKOFF SYNDROME

Arie J. Wester, Josette Westhoff, Roy P.C. Kessels, Jos I.M. Egger

Abstract

Objective: The Montreal Cognitive Assessment (MoCA) provides an indication of overall cognitive functioning and aims to measure several cognitive domains, such as memory, visuospatial abilities, executive function, attention and concentration, language, fluency, and orientation. It has been found sensitive to detect the (mild) cognitive impairment in patients diagnosed with substance dependence but it is unknown whether the MoCA is able to differentiate between mild and more severe forms of memory impairment, such as differentiating Korsakoff patients, who have severe amnesia, orientation difficulties and executive dysfunctions, from chronic alcoholics, who have cognitive deficits, but do not fulfill the criteria for KS.

Method: In order to examine discriminatory power of the MoCA and predictive capacities for the severity of amnesia, both the MoCA and the widely-used Rivermead Behavioural Memory Test (RBMT-3) were administered to 20 patients with Korsakoff syndrome, to 26 patients with non-Korsakoff alcohol related cognitive impairment, and to 33 healthy control subjects.

Results: Results suggests that the MoCA has discriminatory power in the diagnosis of patients with alcohol-related cognitive impairments and predictive capacities with regard to the severity of memory impairment. For all comparisons, specific cut-off scores were established.

Conclusions: While it can be concluded that the MoCA is a useful screening instrument, it should be stressed that it cannot substitute a more extensive neuropsychological assessment which is essential to the detailed analysis of the cognitive profile and, consequently, for adequate treatment selection.

Key words: memory disorder, Korsakoff syndrome, neuropsychological assessment, screening, alcohol use disorder (AUD)

Declaration of interest: the authors declare no competing financial interests

Arie J. Wester,^(1,2) Josette Westhoff,^(1,2) Roy P.C. Kessels,^(1,2,3) Jos I.M. Egger^(2,4,5,6)

⁽¹⁾ Korsakoff Clinic, Vincent van Gogh Institute for Psychiatry, Venray, The Netherlands

⁽²⁾ Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, The Netherlands

⁽³⁾ Department of Medical Psychology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

⁽⁴⁾ Centre of Excellence for Neuropsychiatry, Vincent van Gogh Institute for Psychiatry, Venray, The Netherlands

⁽⁵⁾ Behavioural Science Institute, Radboud University Nijmegen, Nijmegen, The Netherlands

⁽⁶⁾ Pompe Institute for Forensic Psychiatry, Pro Persona, Nijmegen, The Netherlands

Corresponding author

Prof. Jos. I.M. Egger, PhD
Vincent van Gogh Centre of Excellence for Neuropsychiatry
Radboud University Nijmegen
Stationsweg 46, 5803 AC Venray.
Tel. +31.643.213.247; Fax: +31.478.630.797
E-mail: j.egger@psych.ru.nl

Introduction

Memory plays an essential role in everyday tasks, such as speaking, reading, writing, planning, and understanding, and is indispensable for adequate human functioning (Baddeley et al. 2002). Consequently, amnesic disorders are likely to have great impact on almost all areas of daily life. Such disorders can be caused by several neurological and neuropsychiatric diseases such as dementia, brain tumor, stroke, cerebral trauma or Korsakoff's syndrome (Mesulam 2008). The

classification of memory disorders and particularly, the differentiation of milder from more severe forms, not only supports the diagnostic process but is also a prerequisite for selecting interventions fitting the degree of impairment.

Extensive neuropsychological assessment can be used to investigate the profile and severity of cognitive impairments in multiple cognitive domains (Lezak et al. 2012). However, such an assessment may be costly and not feasible in all clinical settings due to time constraints. As a result, screening instruments for the detection of

cognitive impairments have been developed, such as the Mini-Mental State Examination (Folstein et al. 1975). However, many of these screening instruments have been criticized due to lack of sensitivity and specificity or poor reliability (review MMSE). According to Shulman (2000), an ideal screening instrument meets the following criteria: (a) short administration time, (b) easy to score, and (c) adequate levels of sensitivity, specificity, and validity. An example of a promising short screening instrument is the Montreal Cognitive Assessment (MoCA), which provides an indication of overall cognitive functioning (Nasreddine et al. 2005) and aims to measure several cognitive domains, such as memory, visuospatial abilities, executive function, attention and concentration, language, fluency, and orientation.

The MoCA has been found to be sensitive to less severe forms of cognitive disorders that can occur in the context of neurodegenerative diseases (e.g., Mild Cognitive Impairment; MCI) and several studies have showed that the MoCA can distinguish patients with MCI from healthy controls (Nasreddine et al. 2005). However, different cut-off scores have been reported. Fujiwara et al. (2010), for instance, report an optimal cut-off score of 25 (out of the maximum score of 30) for detecting MCI (Fujiwara et al. 2010), while others reported a cut-off score of 23 (e.g., Lee et al. 2008). This might be attributed to differences in educational level of the participants since the number of educational years has been reported to influence performance on the MoCA (Nasreddine et al. 2005). Whether other patient characteristics would lead to different levels of sensitivity and specificity, remains equivocal (Thissen et al. 2010).

Since there is evidence for the MoCA being able to tap mild memory impairments and to adequately classify patients with MCI, it would be useful to know if it can be used for the classification of other patient groups with cognitive disorders, specifically in patients suspect of cognitive impairment due to alcohol-use disorder. The MoCA has been found sensitive to detect the (mild) cognitive impairment in patients diagnosed with substance dependence (Copersino et al. 2009). It remains to be studied, however, whether in these patients with substance dependence, the MoCA is able to differentiate between mild and more severe forms of memory impairment, such as differentiating patients with Korsakoff's syndrome (KS) who have severe amnesia, orientation difficulties and executive dysfunction (Kopelman 2002) from chronic alcoholics who have cognitive deficits, but do not fulfill the criteria for KS.

Korsakoff syndrome can be defined as 'an abnormal mental state in which memory and learning are affected out of all proportion to other cognitive functions in an otherwise alert and responsive patient, resulting from nutritional depletion, notably thiamine deficiency' (Kopelman 2002, p. 2153). In the Western world, Korsakoff syndrome is usually found in chronic alcoholics. Apart from the study of Blansjaar and colleagues (1987), who reported a prevalence of 4.8 per 10.000 inhabitants diagnosed with Korsakoff's syndrome in the city of The Hague, Netherlands, no recent Dutch epidemiological data are available. Based on these data, the number of Korsakoff patients in the Netherlands is estimated between 5.000 and 15.000 individuals.

The present study examines the sensitivity and specificity of the MoCA in a group of participants with suspected memory deficits due alcohol-use disorder, comparing the MoCA with a more extensive assessment

of memory function using the third version of the Rivermead Behavioural Memory Test (RBMT-3) as gold standard. The RBMT-3 is a test battery with high ecological validity, enabling the detection of disorders in everyday memory functioning. In addition, the test measures the severity of a memory disorder, which is of special interest to this study. Its subtests reflect everyday memory tasks, such as memorizing news reports, names, routes, appointments, and recognition of pictures and faces (Wilson et al. 2008). This study has two objectives. First, we examine whether the MoCA can distinguish between two patient groups with cognitive disorders and a healthy control group, and particularly addresses the question to what extent it is able to classify patients with Korsakoff's syndrome and patients with cognitive impairment due to excessive alcohol use. Second, we will examine whether the MoCA can be used as an index of the severity of a memory disorder. Finally, the optimal cut-off scores for the MoCA will be calculated.

Method

Subjects

A total of 79 adults, aged 38-72 years, participated in this study. Patients (n=46) were admitted to the Korsakoff clinic of the Vincent Van Gogh Institute for Psychiatry in Venray, The Netherlands. Reason for admission was suspected cognitive impairments due to alcohol-use disorder. Of these 46 patients, twenty were diagnosed with KS, and 26 subjects with alcohol-related cognitive impairment (not fulfilling the criteria for KS). The KS diagnosis was given when anterograde amnesia was present in a history of chronic, heavy drinking, and malnutrition. KS patients had to fulfill the DSM-IV-TR criteria for alcohol-induced persisting amnesic disorder. The diagnoses were supported by extensive neuropsychological assessment, medical history, psychiatric and neuroradiological examination and observations by a multidisciplinary team, and were agreed upon in a multidisciplinary meeting. All patients with alcohol-related cognitive impairments had a history of long-term heavy drinking, and were referred by addiction care centers. They fulfilled the DSM-IV-TR criteria for alcohol dependence and did not have the severe memory deficits of Korsakoff's syndrome. In addition to these patients, 33 healthy volunteers were included. Potential volunteers with a history of neurological or psychiatric disease, or documented alcohol or drug addictive disorders (self report) were excluded from participation. **Table 1** presents the demographic data of the three groups.

Material

The Dutch version of the Montreal Cognitive Assessment (MoCA-D) is a cognitive screening instrument consisting of 13 short subtests, tapping the following cognitive functions: memory, visuospatial abilities, executive functions, attention and concentration, language, and orientation. Scores range from 0 to 30 and higher scores indicate better cognitive functioning. Administration takes approximately ten minutes. The short-term memory task involves two learning trials of five nouns and a delayed recall after approximately 5 minutes (5 points). Visuospatial abilities are assessed using a clock-drawing task (3 points) and a three-dimensional cube copy (1 point). Executive functions are assessed using an alternation task adapted from the Tail-Making Test B (1 point), a phonemic fluency task (1

Table 1. Demographical variables of healthy adults, patients with alcohol-related cognitive impairments, and patients with Korsakoff syndrome

	Group			<i>p</i>
	Healthy adults	Alcohol related cognitive impairment	Korsakoff syndrome	
<i>n</i>	33	26	20	
Ages in years (<i>Mean ± SD</i>)	53.0 (6.7)	54.5 (8.1)	57.6 (8.7)	.122
Sex (% male)	15 (45.5)	20 (76.9)	15 (75.0)	.020
Level of education (<i>modus ± range</i>)	5 (3-6)	4 (1-6)	3 (2-6)	.010

Note. Education level was assessed using seven categories in accordance with the Dutch educational system. 1= 1-5 years of education; 2= 6 years of education; 3= 7-8 years of education; 4= 7-9 years of education; 5=7-10 years of education; 6= 7-16 years of education; 7= 17-20 years of education (Bouma et al. 2012).

point), and a verbal abstraction task (2 points). Attention, concentration and working memory are evaluated using a sustained attention task (1 point), a serial subtraction task (3 points), and digits forward and backward (1 point each). The subtest language consists of a three-item animal naming task (3 points) and repetition of two complex sentences (2 points). Finally, orientation to time and place is evaluated (6 points). The MoCA includes a correction for educational level by adding one point to the total MoCA score for people with less than 12 years of education (equaling an educational level of less than 5 in the Dutch educational system; Verhage 1964).

The Dutch version of the RBMT-3 was used (Wester et al. 2013) that is composed of 14 subtests belonging to six categories: verbal, visual, spatial, and prospective memory, orientation, and new learning. Remembering two names, and an immediate and delayed recall test of a story form the heart of the verbal memory subtask. Visual memory is assessed by face and picture recognition. Immediate and delayed recall of a route is used to measure spatial memory. Prospective memory involves remembering appointments, personal belongings, and shopping items. Spatial and temporal orientation is also evaluated. Finally, immediate and delayed recall task of a novel complex puzzle is assessed. Raw scores of each subtask were transformed into standard (scaled) scores in accordance with the original test manual (Wilson et al. 2008), taking into account the age of the participant. Afterwards the sum of the scaled scores is converted into a general memory index score (GMI), which has a mean of 100 and a standard deviation of 15. In this investigation GMI is used as a memory measure and higher scores indicate better memory functioning.

The English version of the RBMT-3 has a good construct validity, ecological validity and clinical validity. Wilson and colleagues (2008) provide strong evidence to support that the assessment is sensitive to memory problems. The Dutch version used in this study proves to have good sensitivity and adequate specificity (Wester et al. 2013a). Moreover, this version is a substantial improvement over the original RBMT, as it reduces the problem of ceiling and floor effects and the number of misclassifications (Wester et al. 2013b).

Procedure

Data of the patients were collected from an existing

clinical research data base of the Vincent Van Gogh Institute for Mental Health. Only patients were selected that had completed both the MoCA-D and the RBMT-3. The MoCA-D was administered to the two patient groups at intake by a trained neuropsychologist. Approximately six to eight weeks after admission to the Korsakoff Clinic, the RBMT-3 was administered by a neuropsychology intern during the course of an extensive neuropsychological assessment. The time interval between administration of the MoCA-D and the RBMT-3 was at most three months. The first version of the RBMT-3 was used for Korsakoff patients as well as for patients with cognitive impairment. Results of the MoCA-D were not used for establishing the multidisciplinary diagnosis, thus avoiding the problem of circularity.

The healthy participants were recruited from the personal network of the researchers. Only adults between 40 and 70 years of age and with lower than academic education were invited, in order to match the control group comparable with the patients. If the participants gave consent for participation, an appointment was made for the administration of the tasks. The assessment took place in a quiet room, in order to prevent distraction by environmental stimuli. First they were asked to provide some demographic information. After this the MoCA-D and the RBMT-3 were administered. The duration of the complete assessment was 45 to 60 minutes.

Analysis

To compare the MoCA Total score, MoCA Domain scores, and the RBMT-3 GMI score across the three groups, MANCOVA was performed. Educational level was included as covariate, since the three groups showed slight, yet significant differences on this demographic variable (see **table 1**). Significant differences were further analyzed with Bonferroni-corrected post-hoc tests. ROC analyses were used to examine whether the MoCA differentiates between healthy controls and two patient groups.

To investigate the second question, i.e., the predictive value of the MoCA in relation to the severity of the memory impairment, all participants were divided into three groups based on their RBMT-3 GMI scores. Subjects with severe memory impairment, determined

by a GMI score of at least two standard deviations below the UK normative mean (GMI < 70), were placed in the first group. People with mild memory deficits (GMI 70 – 84) were assigned to the second group and participants with unimpaired memory functioning to the third group (GMI ≥ 85). Subsequently, three ROC analyses were performed to examine the test's sensitivity and specificity. For all performed ROC analyses, optimal cut-off score were defined as those with a sensitivity ≥ 80% and a specificity ≥ 60% (Blake et al. 2002). In case these criteria were not met, the best possible cut-off scores were reported instead.

Results

Table 2 shows the results of the MoCA Total and Domain scores, as well as the RBMT-3 GMI scores for all groups. On the overall measures, significant group effects were found for both the MoCA Total score ($F(2,75) = 30.37, p < .001$) and the RBMT-3 GMI score ($F(2,75) = 52.00, p < .001$). These effects were influenced positively by educational level ($F(1,75) = 17.30, p < .001$ and $F(1,75) = 6.18, p < .001$, respectively). Post-hoc analyses showed that the healthy participants had the highest performance and KS patients performed worse compared to the other groups.

Examination of the MoCA subdomains reveals that only the scores on the subdomain Memory significantly differed between the three groups ($F(2,75) = 33.04, p < .001$) with healthy people scoring highest and KS patients scoring lowest. On the subdomain Executive functioning healthy controls performed significantly higher than the two patient groups ($F(2,75) = 3.23, p < .05$), whereas the latter two performed at an equal level. Only the patients with cognitive impairment obtained a significantly lower score than the healthy controls (F

(2,75) = 7.39, $p < .01$) on the visuospatial tasks. On the subtask Orientation, KS patients scored significantly lower than the two other groups ($F(2,75) = 32.81, p < .001$). Finally, on the two remaining subdomains (Attention and Language), no significant differences were found between the groups ($p = .08$ and $p = .43$, respectively).

Figure 1 shows the ROC curves of the MoCA detecting the three groups of participants. **Table 3** displays an overview of the corresponding cut-off scores. The MoCA Total score significantly differentiated between KS patients and healthy controls ($AUC = .97, p < .001$). An optimal cut-off score of 23 was found (≤ 23 as indicator for KS) with a sensitivity of 88% and a specificity of 95%. Also, MoCA Total score could significantly distinguish patients with cognitive impairment from healthy controls ($AUC = .85, p < .001$). Here, an optimal cut-off score of 24 was detected with a sensitivity of 85% and a specificity of 69% (≤ 24 as indicator for cognitive impairment). For the distinction between the two patient groups, however, no optimal cut-off score could be determined ($AUC = .73, p < .01$). The best possible cut-off score was 20 (≤ 20 as indicator for KS) with a sensitivity of 73% and a specificity of 75%.

Figure 2 shows the ROC-curves of the MoCA for the detection of the three GMI groups. The corresponding cut-off scores are shown in **table 4**. Again, MoCA Total score can discriminate individuals with severe memory impairment from those without memory impairment ($AUC = .96, p < .001$) as well as individuals with mild memory deficits from those without memory impairment ($AUC = .82, p < .001$). For the first comparison, an optimal cut-off score of 23 was found (≤ 23 as indicator for a severe memory impairment; with a sensitivity of 91% and a specificity of 88%) and for the second comparison, an optimal cut-

Table 2. Mean and standard deviations of MoCA-D Total score and Domain scores, and RBMT-3 General Memory Index (GMI) score per group

	Group			F-value	p-value
	Healthy adults (n = 33)	Alcohol related cognitive impairment (n = 26)	Korsakoff syndrome (n = 20)		
<i>MoCA-D Mean score (SD)</i>					
Total score	26.52 (2.0)	22.04 (3.8)###	18.85 (3.7)#####	30.37	< .001
Memory	3.33 (1.0)	2.04 (1.4)###	0.40 (0.8)#####	33.04	< .001
Executive functioning	2.55 (0.8)	1.88 (1.1)#	1.75 (1.1)#	3.23	< .05
Attention and concentration	5.85 (0.4)	5.08 (1.3)	5.05 (1.5)	2.59	.08
Language	4.61 (0.7)	4.19 (0.8)	4.25 (0.8)	0.85	.43
Visuospatial abilities	3.61 (0.7)	2.54 (1.1)###	2.95 (1.1)	7.39	< .01
Orientation	5.76 (0.4)	5.42 (0.8)	3.60 (1.5)#####	32.81	< .001
<i>RBMT-3 Mean score (SD)</i>					
GMI	91.64 (10.5)	78.46 (11.8)###	60.25 (4.4)#####	52.00	< .001

Note. Significant difference with healthy adults: * $p < .05$, ** $p < .01$, *** $p < .001$. Significant difference with alcohol-related cognitive impairment patients: * $p < .05$, ** $p < .01$, *** $p < .001$.

Figure 1. MoCA-D ROC curves for distinguishing Korsakoff syndrome from alcohol related cognitive impairment

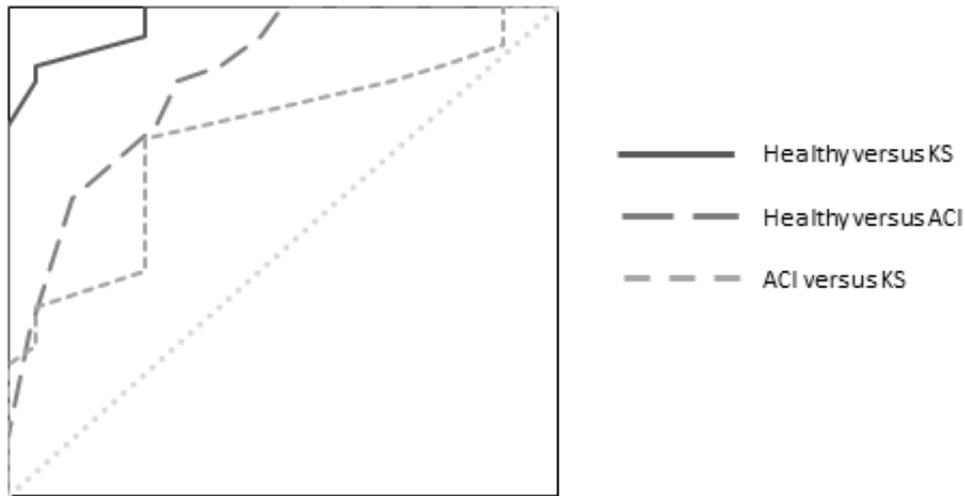


Table 3. Sensitivity and specificity of the MoCA-D for the detection of Korsakoff (KS) and Alcohol related cognitive impairment (ACI)

MoCA-D Cut-off scores	Healthy versus KS		Healthy versus ACI		ACI versus KS	
	sensitivity	specificity	sensitivity	specificity	sensitivity	specificity
18					0.81	0.45
19					0.77	0.60
20					0.73 [#]	0.75 [#]
21	1.00	0.75			0.50	0.75
22	0.94	0.75	0.94	0.54	0.46	0.75
23	0.88*	0.95*	0.88	0.61		
24	0.85	0.95	0.85*	0.69*		
25	0.76	1.00	0.76	0.73		
26			0.61	0.88		

Note. *Optimal cut-off score; [#]best possible cut-off score.

off score of 24 could be established (≤ 24 as indicator for mild cognitive impairment) with a sensitivity of 88% and a specificity of 71%. Finally, individuals with severe and mild memory impairment could also be differentiated ($AUC = .75, p < .01$). A sensitivity of 81% and a specificity of 69% was found in conjunction with an optimal cut-off score of 20 (≤ 20 as indicator of severe memory impairment).

Discussion

This is the first study that examines predictive and convergent validity of the MoCA in a combined sample of KS patients, patients with alcohol-related cognitive impairment not fulfilling the criteria for KS, and

healthy individuals. The MoCA was able to distinguish between these three diagnostic classification groups, and also between subgroups based on three levels of memory impairment based on the RBMT-3 GMI score. These findings are in agreement with previous studies showing that (everyday) memory is more affected in Korsakoff patients than in the patient group with cognitive impairment, compared to healthy controls. The MoCA memory score was the only subdomain on which all three groups differed significantly.

Main aim of this study was to examine the diagnostic accuracy of the MoCA. Previous research already showed that the MoCA is able to differentiate MCI and Alzheimer dementia from healthy controls (Freitas et al. 2013, Fujiwara et al. 2010, Lee et al. 2008, Luis et al. 2009, Nasreddine et al. 2005). Furthermore, the MoCA

Figure 2. MoCA-D ROC curves for distinguishing mild from severe memory disorders

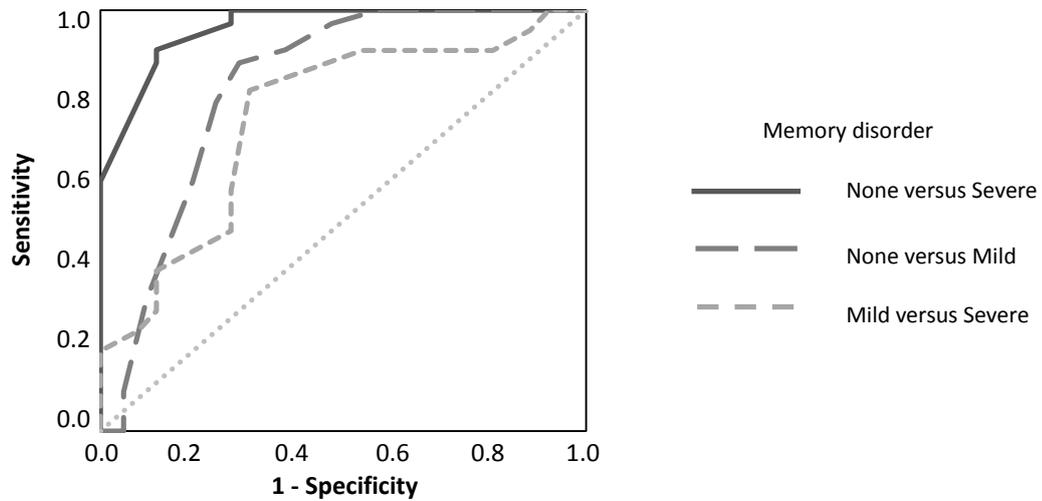


Table 4. Sensitivity and specificity of the MoCA-D for the detection of mild and severe memory disorders

MoCA-D Cut-off scores	None versus Severe		None versus Mild		Mild versus Severe	
	sensitivity	specificity	sensitivity	specificity	sensitivity	specificity
18					0.91	0.46
19					0.86	0.58
20					0.81*	0.69*
21	1.00	0.73			0.57	0.73
22	0.97	0.73	0.97	0.52	0.48	0.73
23	0.91*	0.88*	0.91	0.62		
24	0.78	0.88	0.88*	0.71*		
25	0.78	0.92	0.78	0.76		
26			0.59	0.81		

Note. *Optimal cut-off score.

is able to classify cognitive dysfunction in patients with substance dependence (Copersino et al. 2009). These results coincide with findings of the present study that showed the MoCA Total score to be able to distinguish chronic alcoholics with cognitive impairment (non-KS) from healthy controls, with an optimal cut-off score (≤ 24) that had adequate sensitivity and specificity. The same was true for KS patients (cut-off score of ≤ 23).

Although the MoCA appears to have adequate diagnostic accuracy in the present sample, a note of caution should be mentioned here. While the MoCA is able to classify the two patient groups compared to controls, the discriminatory power of the MoCA seems to be moderate when comparing the two patient groups directly. The best possible cut-off score for distinguishing these two groups (≤ 20) had a sensitivity

and specificity of 73% and 75%, respectively, indicating that about 27% of the KS patients is classified as a non-KS patient whereas, 25% of the non-KS patients is classified as having KS. Based on these findings, extensive neuropsychological assessment may have an added value to determinate the adequate diagnosis (KS vs. Alcohol-related cognitive impairment). For the prediction of memory impairment severity by means of the MoCA, promising results were found. The MoCA is able to distinguish between people with no, mild or severe cognitive impairment, with good sensitivity and specificity. Unlike most previous studies, the present research also compared the mildly and severely memory-impaired groups directly, showing a high discriminatory power of the MoCA for these two patient groups.

The question arises how these findings translate into clinical practice. Given the emergence of optimal cut-off scores, the MoCA is able to predict the severity of memory impairment in a sample of cognitively impaired patients with alcohol-use disorder. Still, in cases with MoCA scores between 20 and 24, it is more difficult to adequately classify memory impairment severity since in this score interval, both severe memory impairment and mild memory impairment are included. In other words, a score in this range signals that a memory impairment is present, but cannot differentiate its severity, requiring more extensive neuropsychological memory testing.

Several limitations of this study have to be mentioned. First, in both patient groups, the MoCA was administered during admission to the clinic. For the majority of patients, alcohol abstinence could not be guaranteed at that point in time. Some studies report that cognitive impairments in alcoholics persist after a short period of abstinence (Block et al. 2002, Munro et al. 2000). However, others suggest that some recovery of cognitive functioning is possible after a period of abstinence (Bates et al. 2005, Oscar-Berman et al. 2004, Walvoort et al. 2013). Taking into account that the RBMT-3 was administered after a period of abstinence (i.e., more than 6 weeks after admission), it is possible that the two patient groups scored lower on the MoCA when compared with scoring levels on the RBMT-3. Moreover, a slight difference in educational level was detected in the three groups. Bearing in mind that educational level has a positive influence on cognitive abilities (Acevedo et al. 2007, Ganguli et al. 2010), the elevated scores of the healthy controls could be partially explained by their higher educational level, although inclusion of education level as a covariate still resulted in significant between-group differences. Finally, this specific study investigated only to what extent the MoCA is able to predict the severity of memory impairment. Future research will have to address the validity claim for other cognitive domains.

In sum, results from the present study suggests that the MoCA has discriminatory power in the diagnosis of patients with alcohol-related cognitive impairments and predictive capacities with regard to the severity of memory impairment. While it can be concluded that the MoCA is a useful screening instrument, it should be stressed that it cannot substitute a more extensive neuropsychological assessment, as this also covers other cognitive domains and uses validated tests for the assessment of specific sub-processes within a domain (e.g., is able to differentiate memory encoding from retrieval). The latter is often essential for establishing a detailed analysis of the cognitive profile, which in turn is vital for adequate treatment selection, especially in relation to interventions using cognitive rehabilitation principles.

Acknowledgements

The authors report no conflicts of interest in this work. The MoCA-D is available for free from www.mocatest.org. We thank Pearson Assessment B.V., Amsterdam, The Netherlands, for providing the RBMT-3 test materials and for authorizing the Dutch translation.

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