

Research Article

Use of the MoCA Combined with the Fab for the Screening of Cognitive Dysfunction in Patients with Alcohol Use Disorders

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Abstract

Objective: Cognitive dysfunction is common in patients with Alcohol Use Disorders (AUD). This impairment needs to be detected since it affects the quality of life of patients and compliance with therapeutic programs.

As global cognitive and executive functions may be differently affected in AUD patients, we wondered whether, when diagnosing cognitive dysfunction, specific measurement of executive functioning could provide an incremental value that could be used in addition to global cognitive measurement.

Methods: Cognitive status was evaluated at admission using the Montreal Cognitive Assessment (MoCA) test, the Frontal Assessment Battery (FAB) and a battery of Neuropsychological (NP) reference tests in 134 patients with AUD hospitalized in an addictions treatment unit.

Results: Seventy patients (52%) had cognitive dysfunction according to the battery of Neuropsychological (NP) tests. Among these 70 patients, 59 (84%) and 38 (54%) had abnormal MoCA and FAB test results, respectively. Concordance between the MoCA and the FAB was weak ($\kappa = 0.27$). Analysis through logistic regression showed that the Area under Curve (AUC) obtained with the MoCA test was a better single predictor of cognitive impairment (0.85) than that obtained with the FAB (0.73). Combining the two tests produced an AUC of 0.86, a value not significantly different from that obtained with the MoCA.

Conclusions: The MoCA-FAB combination did not perform better than the MoCA alone as a screening tool for cognitive dysfunction among AUD patients. This confirms that the MoCA is an efficient screening tool since it can detect frontal as well as general cognitive disorders.

Introduction

Cognitive dysfunction is common in patients with alcohol use disorders (AUD), varying from 50 to 70% according to published series [1-3]. This dysfunction impairs quality of life, leads to misunderstandings and poor recall of therapeutic advice, and decreases treatment compliance [4,5].

Cognition is a term that includes a large range of brain abilities such as executive functions, language, memory, attention and abstraction [6]. Executive function is considered to encompass three major skills, *i.e.*, inhibition, working memory and cognitive flexibility [7].

In patients with AUD, several areas are affected by neurological injury, with the most specifically affected area being the frontal lobe. Abnormal functioning in specific neural networks related to executive function in the Prefrontal Cortex (PFC) is frequently observed and processes such as self-control and behavior monitoring, emotion regulation, motivation, awareness, attention and flexibility, working memory, and learning are frequently impaired [8,9]. These executive dysfunctions have a clinical impact as they may be predictive of poor outcomes following drug addiction treatment [10]. Studies have shown that frontal lobe deficiency characterized by executive

dysfunction including attention and working memory deficits has been associated with an inability to abstain from alcohol and negative clinical implications [11,12].

Overall, in AUD, cognitive dysfunction is associated with a negative prognosis. That is why screening for cognitive dysfunction in AUD patients is essential for tailoring treatment programs. Screening tests have been evaluated for that purpose, including the MoCA [13] and the BEARNI [14].

However, global cognitive and executive functions may be differently affected by chronic use of alcohol [12]. As alcoholics with significant deficits in executive functions may have preserved global cognitive function [15]. Therefore, screening of cognitive dysfunction in AUD patients should also take into account the possibility of specific frontal dysfunction. For this concern currently available screening tools, such as the MoCA, which is commonly used in AUD patients, may be insufficient. Indeed, in the MoCA, only 10 points among a total of 30 are devoted to executive functions (Visuospatial/executive: 4 points; Attention: inverse repeat: 1; list of letters: 1, subtraction: 3; Language fluency: 1). This led to questioning about whether it might be useful to use a specific screening tool for frontal dysfunction together with a global test such as the MoCA.

One of these specific tools is the Frontal Assessment Battery (FAB). It was developed as a short bedside cognitive and behavioral battery to assess frontal lobe function [16]. And is therefore a good tool for the assessment of dysexecutive disorders [17]. Showed that the FAB is a valid neuropsychological tool for the assessment of executive cognitive function in substance drug users. It is very quick and easy to administer (paper-and-pencil) and is useful in daily practice.

One of the main focuses of our addiction treatment unit is the detection of cognitive dysfunction and its improvement through specific therapeutic programs. Each hospitalized patient therefore undergoes cognitive tests at admission. We use two screening tools administered in a random order: the MoCA and the FAB. When either or both of the test results are abnormal, the results are confirmed by a neuropsychological battery. This battery was also systematically administered to patients included in two research protocols [6,18]. Regardless of the results of the screening tests.

The objective of this research was to assess whether measurement of executive functions would provide an incremental value that could be used in addition to global cognitive measurement for the diagnosis of cognitive dysfunction in alcoholic patients. We expected that the distinction between AUD patients with no cognitive dysfunction and those with one or more cognitive disorders would be improved by combining FAB and MOCA global scores compared to the MOCA global score alone.

Patients and Methods

This study consisted in the secondary analysis of a database obtained by merging data obtained in 2 previous studies in which cognitive status was evaluated at admission using the MoCA and a battery of neuropsychological reference tests [6,18]. The FAB was also administered but was not analyzed. These two studies were carried out in the addictions treatment unit of the University Hospital of Nîmes. The inclusion and exclusion criteria as well as the methods used were similar in both studies.

Patients

The inclusion criteria in this study were as follows: admission for severe AUD assessed by the DSM-5 criteria (American Psychiatric Association, 2013); age above 18 years; no present drug consumption except tobacco before admission (assessed by declarative data and urinary tests performed at admission); ability to understand and speak French; oral agreement to participate.

The exclusion criteria were severe comorbid neurological or psychiatric disease such as dementia, Alzheimer's disease, or psychosis; past history of neurological disorders such as head injuries, with loss of consciousness for longer than 30 min; encephalopathy; history of heart disease; infection by HIV. None of the patients included in the study had participated in another research program.

The following sociodemographic data were recorded: age, sex, education level (equal to or higher than 12 years), family history of alcohol/drug use disorders through a family tree, and smoking status. Mean alcohol consumption was evaluated using the Timeline Followback [19]. Cannabis, cocaine, and heroin consumption were recorded based on declarative data and urinary tests.

Methods

The MoCA test: We used the 7.1 version of the MoCA translated into French by the MoCA test organization ([http:// www.MoCAtest.org/](http://www.MoCAtest.org/)). The MoCA includes 13 tasks measuring the following 8 cognitive domains: visuospatial skills/executive function, naming, immediate memory (not scored), attention (3 different items with separate scoring), language (2 different items with separate scoring), abstraction, delayed recall, and orientation. A total score is calculated by summing the scores of the 13 tasks. The maximum score possible is 30 points. The normal value in AUD patients is ≥ 26 and the score does not need to be corrected in those with a low education level [6]. The test was administered during the first week following alcohol withdrawal by experienced occupational therapists or neuropsychologists familiar with the test. They all used a similar scoring grid defined in accordance with proposed guidelines [20]. The test was administered in a quiet room in the morning. If the patient was a smoker, he/she was asked to refrain from smoking during the 30 minutes preceding the test in order to avoid any bias related to the acute effect of nicotine [21].

The FAB test: The FAB evaluates general executive functioning such as abstraction/conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control and environmental autonomy [16,17]. Performance on the six subtests of the FAB gives a composite global score, which evaluates the severity of the dysexecutive syndrome and suggests a descriptive pattern of executive cognitive functioning in an evaluated patient. The maximal score is 18 and normal values are ≥ 16 [16].

The battery of neuropsychological tests: The battery of neuropsychological tests comprises the French versions of validated tests already used in previous cognitive studies in alcoholic patients [22-24]. Which specifically assess functions known to be impaired in AUD patients and which are evaluated in the MoCA test, *i.e.*, the Trail Making Test, TMT [25]. Version adapted by Godefroy and the *Groupe de Réflexion pour l'Évaluation des Fonctions Exécutives* (Reflection Group for the Evaluation of Executive Functions [26]. The Stroop test [27]. Version adapted by the [26]. The adapted version of the fluency test [28]. The verbal episodic memory test, (the adapted French version of the Free and Cued Selective Reminding Test (FCSRT) [29]. The California Verbal Learning Test [CVLT] [30]). Attention and working memory (the Digit Span subtest of the Wechsler Adult Intelligence Scale [31]); visuospatial skills (the Rey-Osterrieth Complex Figure, [ROCF] [32]).

The raw result of each test was transformed into either a z-score or a percentile. A score at a task was considered abnormal when the z-score fell 1.65 Standard Deviations (SD) below norms corrected for age, education, and sex, or below the 5th percentile. A cognitive domain was considered impaired when at least one of the corresponding test scores deviated from normal. Patients with one or more cognitive impairment were referred to the "cases" group, patients with no cognitive impairment were referred to the "control group".

Test administration: About 7 to 10 days after alcohol withdrawal, patients were administered the MoCA and the FAB in a random order. The tests were administered in a quiet room in the morning by occupational therapists or neuropsychologists experienced with

the test. Patients were seated and had not smoked recently. The day following these tests, all the patients were administered the neuropsychological test battery by a neuropsychologist.

Statistical analysis

Our objective was to test the hypothesis that use of the MoCA test combined with the FAB test allowed more accurate separation of cases from controls than the MoCA test alone. For this purpose, patients with no cognitive impairment assessed by the neuropsychological battery were coded “0” and patients with one or more cognitive problems were coded “1”. The codes were used to obtain a numeric response vector. Two additional vectors (predictors) generated the total score for either the MoCA or the FAB for each patient. These three vectors contained 134 observations each. We used the ROC function in the *pROC* package for R to compute the AUC and the 95% Confidence Interval (CI). We pursued our analyses by computing the 95% CI of sensitivity and specificity for several threshold values. Confidence intervals (95% CI) were computed with 2000 stratified bootstrap replicates. For this, we used the *ci.thresholds* function in the *pROC* package. We finally searched for threshold values that maximized both sensitivity and specificity as returned by the *coords* function and the Youden’s J index (= sensitivity+specificity-1) [33].

The main objective of our research was to estimate an incremental value for the MoCA and the FAB tests for separating cases from control. For this purpose, we used logistic regression (the *glm* function) to model the dichotomous variable “Groups” (*i.e.*, cases vs. controls). We tested three models: 1) in the first, the MoCA test was modeled as a fixed-effect parameter, 2) in the second, the FAB test was modeled as a fixed-effect parameter, and 3) in the third, both the MoCA and FAB tests were modeled as fixed-effect parameters. We reported regression coefficients and associated p-values. We estimated the quality of our models’ fits using Akaike’s Information Criterion (AIC). We then ran a ROC curve using the probability values returned by the *glm* function. We obtained three AUC values – one for each of the three models mentioned above. We used the *roc.test* function to compare the AUC values obtained from the first and the third models. We chose Delong’s Z test to test the difference between two correlated ROC curves [34]. We used Pearson’s correlation to estimate the relationship between two continuous measures and Student’s t-test to compare two means.

The concordance between the MoCA and the FAB classification (cognitive trouble, yes or no) was measured using the kappa test.

Results

Socio-demographic and addiction data

Among the 146 patients that were included in the initial studies, the FAB was incomplete on admission in 12 cases. Consequently, 134 patients, 97 men (72.4%) and 37 women (27.6%), were finally included in the actual study. Their main characteristics are presented in the (Table 1).

Baseline cognitive evaluation

In this series, 70 patients (52%) presented cognitive dysfunction according to the battery of Neuropsychological (NP) tests (40 patients had mild disorders and 30 patients had severe disorders),

Table 1: Main sociodemographic and addiction characteristics of the 134 patients studied.

N	134
Sex (M/W)	97/37
Age (years)	48.8 ± 9.4
Education (%)	
≤12 years	77.6
>12 years	22.4
Employment (%)	35.1
Smoker (%)	79.1
Cannabis user (%)	14.1
Alcohol (g/day)	227±115
Duration of AUD (years)	15±9
Age at AUD beginning	32.8 ± 11.3
Past family history of AUD (%)	46.7

Table 2: MoCA and FAB results according to the NP battery results.

NP test Impairment N		MoCA score abnormal	FAB score abnormal
No	64	17 (26.6%)	17 (26.6%)
Yes	70	59 (84%)	38 (54%)
Moderate	40	32 (80%)	16 (40%)
Severe	30	27 (90%)	22 (73.3%)

Table 3: Cross-table showing MoCA and FAB test results as a function of NP test results.

NP tests	MoCA test	FAB test		Total
		normal	abnormal	
No disorder (N=64)	normal	35	12	47 (73.4%)
	abnormal	12	5	17 (26.6%)
	Total	47 (73.4%)	17 (26.6%)	64 (100%)
At least one disorder (N=70)	normal	9	2	11 (15.7%)
	abnormal	23	36	59 (84.2%)
	Total	32 (45.7%)	38 (54.2%)	70 (100%)

while 64 patients (48%) presented no abnormalities. Among patients with cognitive impairment diagnosed by the test battery, 59/70 had abnormal MoCA results (84%) and 38/70 had abnormal FAB results (54%) (Table 2). The mean MoCA score was significantly lower ($p < 0.001$) in the sub-group of patients with abnormal NP tests (22.77 ± 3.14 vs 26.37 ± 2.30) as was the case for the FAB test (15.12 ± 1.83 vs 16.38 ± 1.45) (data not shown).

Among the 64 patients in whom the NP tests were normal, 17 had either an abnormal MoCA or an abnormal FAB test (Table 3), indicating a 26.5% false-positive rate. Conversely, in the subjects with at least one abnormal NP test ($N = 70$), the false-negative MoCA test rate was 15.7% while it was 45.7% for the FAB test. Moreover, among the 11 patients with a normal MoCA test, only 2 had an abnormal FAB test, representing a correction rate of 2.8% (2/70). Finally, the concordance between the MoCA and FAB tests was weak ($\kappa = 0.27$).

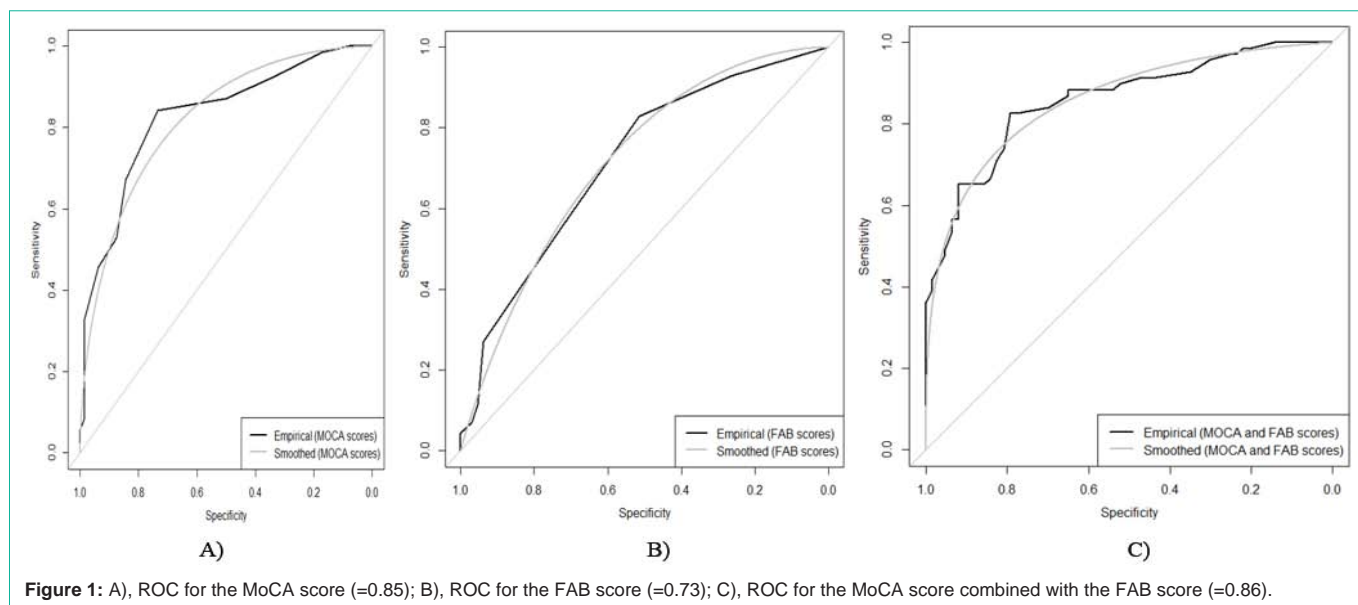


Figure 1: A), ROC for the MoCA score (=0.85); B), ROC for the FAB score (=0.73); C), ROC for the MoCA score combined with the FAB score (=0.86).

Table 4: Relationships between the MoCA score, the FAB score and ancillary executive functions tests (TMT-B = time of completion of the TMT part B; Stroop time = time of completion of the Word-Color part of the Stroop task).

	MOCA	FAB	P Fluency	Animal Fluency	TMT-B	Stroop Time	Stroop interference
MOCA	-						
FAB	.45 ***	-					
P Fluency	.47 ***	.41 ***	-				
Animal Fluency	.28 **	.44 ***	.51 ***	-			
TMT-B	-.43 ***	-.58 ***	-.30 **	-.44 ***	-		
Stroop Time	-.10 N.S.	-.34 ***	-.26 *	-.41 ***	.32 **	-	
Stroop Interference	-.07 N.S.	-.10 N.S.	-.12 N.S.	-.12 N.S.	.23 *	.06 N.S.	-

*p ≤0.05; **p ≤0.01; ***p ≤0.001.

FAB and MoCA correlations with the different tests of the gold standard battery

The FAB score correlated positively with the P Fluency ($r = 0.41$; $p < 0.001$) and animal fluency tests ($r = 0.44$; $p < .001$), and negatively with the time of completion of the TMT-B ($r = -0.58$; $p < .001$) and the Word-Color part of the Stroop task ($r = -0.34$; $p = 0.002$). A non-significant correlation was recorded between the FAB score and the Word-Color part of the Stroop task interference measure ($r = -0.10$; $p = 0.38$).

The MoCA score correlated positively with the P Fluency ($r = 0.47$; $p < 0.001$) and animal fluency tests ($r = 0.28$; $p = 0.01$), and negatively with the time of completion of the TMT-B ($r = -0.43$; $p < 0.001$). Non-significant correlations were recorded between the MoCA score, the time of completion of the Word-Color part of the Stroop task ($r = -0.10$; $p = 0.37$) and the related interference measure ($r = -0.07$; $p = 0.52$). The relationships between the MoCA score, the FAB score and ancillary executive functions tests are presented in (Table 4).

The MoCA and FAB combination

In the first model (AIC = 129.06), we treated the intercept and the MoCA score as fixed effects and reported a negative and significant effect of the former on the probability of being diagnosed with one or more cognitive problems ($B = -0.59$; $p < 0.001$). In the second model

(AIC = 163.97), we treated the intercept and the FAB score as fixed effects and reported a negative and significant effect of the former on the probability of being diagnosed with one or more cognitive problems ($B = -0.59$; $p < 0.001$). In the third model (AIC = 127.73), we treated the intercept, the MoCA score and the FAB score as fixed effects. We confirmed a negative and significant effect of the MoCA on the probability of being diagnosed with one or more cognitive problems ($B = -0.53$; $p < 0.001$), but the effect of the FAB score was not significant anymore ($B = -0.29$; $p = 0.08$).

We next estimated the AUC value of our three logistic regression models. We confirmed that Model 1 with the MoCA as the single predictor produced a higher AUC value (AUC=0.85) (Figure 1A) than Model 2 with the FAB score alone (AUC=0.73) (Figure 1B). The AUC increased (Model 3) when the MoCA and FAB scores were combined (AUC=0.86) (Figure 1C) but the difference with the AUC value obtained with Model 1 was not significant ($Z = -0.81$; $p = 0.42$).

Discussion

The aim of this study was to evaluate use of the FAB combined with the MoCA test as a screening tool for cognitive dysfunction in patients with AUD. The MoCA test has been reported to be efficient for cognitive screening in AUD patients [2]. But it is a rather general test which does not focus strictly on executive functioning disorders.

Given that in some AUD patients executive functions are more affected than non-executive functions such as language, denomination, and abstraction [15]. The MoCA test might produce false results. Therefore, combining it with a specific executive functions screening test, such as the FAB, could improve the screening rate of cognitive disorders.

However, our results show that the MoCA-FAB combination did not perform significantly better than the MoCA alone for the screening of cognitive disorders in AUD patients. In the sub-group of patients with cognitive disorders assessed by the NP test battery, administration of the FAB in patients with a normal MoCA test improved the screening rate by only 2.8%. Moreover, for the MoCA and the MoCA+FAB, AUC were not significantly different, *i.e.*, 0.85 and 0.86, respectively.

This was surprising since, although only few studies have evaluated the FAB in addiction and particularly in AUD, their results suggested that the FAB test was efficient for screening frontal disorders in these patients. A Brazilian study evaluated 32 patients who were heavy alcohol users, but the primary inclusion criterion was dependence on cocaine [17]. The FAB was informative in this series since 3 of the 6 cognitive domains assessed (abstract reasoning, motor programming, and cognitive flexibility) were impaired compared to the control group [12]. Evaluated 60 AUD patients comparable to ours, of which most were men (87%) with significant mean daily alcohol consumption (28 units per day versus 22 in our series), and only a minority (12%) had completed higher education. In this work, the mean FAB score was very low at 11.1. [35], 42 patients undergoing alcoholic detoxification were included in 2 different groups based on MOA B platelet activity values. The mean FAB values in these 2 groups were close to our results at respectively 16.2 and 15.8, although the subjects' mean alcohol consumption was lower (130 and 95 g/d respectively) and they had been abstinent for slightly longer (112 d and 98 d in each group, respectively) than the subjects in our series.

Finally, it was reported that the FAB has good psychometric properties (internal consistency, optimal interrater reliability, and concurrent validity) and that it allowed around 90 % of cases to be correctly identified in a discriminant analysis of patients and controls [16].

Analysis of our results indicates that the FAB alone predicts the probability of being diagnosed with one or more cognitive problems, but this effect turned to be not significant when the MoCA was included in our model. The absence of significant screening improvement by use of the MoCA combined with the FAB may therefore be related to the fact that the information provided by FAB is already provided by the MoCA score. Indeed, both the MoCA and FAB correlated significantly with several tests of the gold standard battery, *i.e.*, P Fluency, the animal fluency test and the time of completion of the TMT-B. Furthermore, neither the MoCA nor the FAB were correlated with the Word-Color part of the Stroop task interference measure. The only significant discordance observed between the MoCA and the FAB was the correlation between the FAB score and the Word-Color part of the Stroop task.

As stated above, the MoCA test covers more cognitive domains than the FAB. In our series almost all patients with abnormal FAB results also had abnormal MoCA results, and as the screening

performance of the MoCA test is better than the FAB, this suggests that in a subset of AUD patients, cognitive disorders might involve global rather than only executive functions, in accordance with other reports [12,15].

In conclusion, our results showed that the MoCA-FAB combination did not perform better than the MoCA alone as a screening tool for cognitive dysfunction among AUD patients. This confirms that the MoCA is a very interesting screening tool in this population and its design makes it possible to detect frontal as well as general cognitive disorders.

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