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Executive Functions and Screening for Mild Cognitive Impairment and Alzheimer's Disease: A Cross-Sectional Study

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Abstract

Context: Subjective memory complaints, before mild cognitive impairment (MCI), constitute the chief symptoms during the development of Alzheimer's disease (AD) and are generally the initial signs for identifying the disease.

Objective: The objective was to explore executive functions capacities in differentiating patients with AD from those with MCI as well as from that exempt from any cognitive deficit (CO). This study enabled us to compare the cognitive and specifically executive functioning of three participant groups (AD, MCI and CO) to determine an optimal measure(s) for differential diagnosis.

Methods: A total of 116 participants were recruited (32 AD, 40 MCI, and 44 CO). To estimate executive function capacities, the Clock Drawing Test (CDT), the Trail Making Test Part A and B (TMT A and B) as well as the Verbal Fluency Tests - Alphabetic (VFT-A) and Category (VFT-C) were used. To exclude patients with depression, the Geriatric Depression Scale (GDS) with cut-off score was used. Furthermore, the Mini Mental State Examination (MMSE) was used to make between groups comparison on general cognition.

Results: A significant mean score difference was observed between the MCI and CO groups on all executive function measures, except for the VFT-A. In contrast to other groups, the AD group performed significantly worst on all executive function measures.

Conclusion: Herein, a significant difference between AD, MCI, and CO groups on executive functioning tasks, where AD group underperformed was reported. This warrants the use of executive functioning assessment as a way to help differential diagnosis.

Keywords: Alzheimer's disease; Cognitive impairment; Executive functions; Screening; Neuropsychology

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Introduction

Subjective memory complaints, before mild cognitive impairment (MCI) [1], constitute the chief symptoms during the development of Alzheimer's disease (AD) and are generally the initial signs for identifying the disease [2]. At first, short-term memory is affected, where the patient presents with difficulty in remembering recent events yet remembers events from a distant past relatively well. MCI patients usually present with cognitive deficits that are not severe enough to reach the diagnostic criteria of AD [3]; and these symptoms can be detected once the prodromal form of dementia stage has begun [4]. By tautology, since the symptoms observed in individuals with MCI are similar to those of mild AD, this could help identifying people at risk for developing AD [5].

During the AD development, amnesic alteration becomes increasingly significant and acts in a retrograde by progressively altering older memories [6]. In a patient with MCI, the overall functioning is not affected and not significant to appear within assessment of activities of daily living [7]. Studies suggest that the presence of psychological distress, when manifested in patients with MCI by symptoms of anxiety and depression, could predict

the progression of MCI towards dementia [8]. Individuals with MCI are at risk of converging towards AD at an annual rate of 10 to 15% [9], a rate that is ten times higher than seen in the general population [10].

Assessment of global cognitive abilities, and specifically executive functions, episodic memory, visual recognition memory, verbal memory, abstract thinking and speed of perception are the most accurate factors for identifying people at risk of developing AD [11-13]. It would appear that the first cognitive domain to be altered during the progression of AD, well before memory, and language and visuo-spatial functions, is the executive functioning [14,15]. Executive functions include a wide array of cognitive processes [16]. However, they remain closely dependent on other major components of the cognitive repertoire, principally attention, language and memory [17].

That executive functions, also interchangeably used as intelligence, are perceived as unitary constructs or not has been frequently debated [18]. Some researchers consider executive functioning as a set of distinct functions that are only inter-related. Moreover, they associate the concept of working memory with an executive function that controls cognitive performance (the so called cognitive-control system) [19]. Others have noted that executive functions share a common component, i.e. executive attention [20].

The link between executive functions and certain cognitive deficits in the early stages of AD or signs of MCI is no longer in doubt, considering the large amount of literature to that effect. However, their precise relation with the working memory rises controversies given the difficulty for conceptualization, wherein lies the disagreement among certain researchers. Evidence shows that it is difficult to completely separate executive functions as the performance of selected tasks, as they can be masked by the so-called "non-executive functions", operated by visuo-spatial processing and language [18]. They manifest themselves by operating on other cognitive processes, thus rendering their studying difficult. Moreover, a table of correlations drawn from analyses made by Miyake et al. [21] shows the close relation between short-term memory and visuo-spatial working memory (r=0.71), spatial visualization (r=0.90), spatial relations (r=0.80) and speed of perception (r=0.71) with respect to executive functions.

Various measures focused on the screening and assessment of cognitive functioning [22]. Among the best screening instruments for cognitive impairment, the General Practitioner Assessment of Cognition (GPCOG), the Mini-Cog and the Memory Impairment Screen (MIS) are recommended for detection cases [23]. However, the Clock Drawing Test (CDT) and the Montreal Cognitive Assessment (MoCA) have gained wide credibility due to their improved sensitivity, as well as their reduced cultural and educational bias susceptibility [22]. Nevertheless, the Mini-Mental State Examination (MMSE) remains the most frequently used cognitive screening instrument [22]. The Trail Making Test (TMT) is a widely used neuropsychological measure for evaluating executive functioning [24]. This test also has good psychometric qualities, especially with test-retest reliability ranging from 0.79 to 0.89 for parts A and B, respectively [25]. The Verbal Fluency Tests - Alphabetic (VFT-A) and Category (VFT-C) are considered as measures for the evaluation of executive functioning [26,27]. These tests have a high internal consistency of 0.83 [28] as well as a good test-retest reliability, generally above 0.70 [29]. Of note, these cognitive measures have different sensitivities for different age and education levels [12]. On a different note, evidence shows the association between depression and subjective memory complaints [30,2].

Several studies explored the utility of executive dysfunctions in patients with AD, but few have considered a mixed battery of neuropsychological tests capable of measuring these functions and easily identifying, differentiating patients with AD from those with MCI and from the participants in a control group by controlling for the effects of age, education and depression symptoms [31]. Thus, this study seeks to determine, among various executive functioning measures, those that distinguish patients with MCI from those with AD in order to facilitate early AD management.

Method

Participants

A total of 116 Canadian (English and French speaking) participants took part in this study, of which 72 had a diagnosis of MCI or AD, and 44 were independent or semi-independent with no diagnosis of MCI or AD. As a whole, there were 69 women and 47 men, with an average age of 75.89 years old (between 59 and 96 years old, standard deviation of 8.82 years). The participants with a diagnostic of MCI or AD were recruited from the Geriatric Department of the Moncton Hospital, in New Brunswick. Those with no diagnosis of MCI or AD were recruited from independent and semi-independent senior's residences in New Brunswick and through calls for participants at events aimed at seniors.

Measures

The basic demographic variables, including date of birth, sex, marital status and education level, cognition and executive functions were assessed through the tests presented hereafter. The French and English versions of the questionnaires were available and used as needed.

Overall cognitive functions

The 1975 Mini-Mental State Examination (MMSE) from Folstein, and colleague [32] was used for the basic assessment of general cognitive functions. The MMSE is designed to screen for, distinguish and quantify the cognitive deficits that a person can present when afflicted by a neurodegenerative disease [33]. It contains 11 items in 2 sections, for a total of 30 points. It is administered individually and takes from 5 to 10 minutes on average. The first section includes temporal orientation, spatial orientation, learning, attention and calculation. The second section covers retention, language, and visuo-constructive abilities [34]. A score of 23/30 is largely accepted as marking the limit between individuals with and without cognitive impairment [35]. A score between 27 and 30 is considered normal cognitive

functioning. A score of 21 to 26 is recognized as mild cognitive impairment: between 11 and 20 as moderate impairment, and below 10 as severe impairment. In 1992, Tombaugh and McIntyre [36] demonstrated an internal consistency of 0.96 for patients with dementia and 0.78 for people in the general population. They also presented good test-retest correlations (reliability), *r*=0.74 to 0.99, for demented and non-demented individuals, respectively.

Executive functions

The 1958 version of the *Trail Making Test* by Reitan [37] is comprised of two parts, form A (TMT-A) and form B (TMT-B). It seeks to evaluate aspects of sustained attention, processing speed and executive functions [24]. Canadian norms are available for both parts of the test [28], as well as for a French-speaking population [38]. It has good psychometric qualities, especially test-retest reliability ranging from 0.79 to 0.89 for parts A and B respectively [25].

The *Verbal Fluency Tests - Category and Alphabetic* (VFT-C and VFT-A) parts are assessing executive dysfunction [26,27]. The two tasks have American demographic norms associated with age, education and ethnicity [39]. The tests have a high internal consistency of 0.83 [40], as well as good test-retest reliability, generally above 0.70 [25,29].

Executive functions and visuo-constructive abilities

The *Clock Drawing Test* (CLOC) that is a measure of executive functions and visuo-constructive abilities [41] was administered and scored as per the method suggested by Shulman [42]. Shulman's scoring system comprises of five levels where 5 represents a perfect clock; 4, minor visuo-spatial errors; 3, good visuo-spatial organization, but a representation 11:10 mistaken; 2, difficulties and moderate disorganization of the time and numbers; and 1, the impossibility of making a reasonable representation of a clock. Ruchinskas and Curyto [43] demonstrated a test-retest reliability varying from 0.70 to 0.94 with different clinical populations, which can be considered excellent at the limit. Also, its inter-administrator reliability was demonstrated to be excellent, reaching *r*=0.97. Similarly, an adequate criteria validity-evidence was reported for CLOC, correlating positively with the measure of independent Functional Independent Measure- cognitive subscale (FIM-Cog) (*r*=0.51) and the MMSE (*r*=0.59).

Depressive symptoms

The 30-items Geriatric Depression Scale (GDS) from Yesavage et al. [44], with a dichotomous (yes/no) response approach was used to explore the possibility of major depression disorder by the DSM criteria, to minimize the possibility of depression symptoms affecting our result. A normal affective state is generally characterized by a score ranging from 0 to 9; a mild depressive state, by a score ranging from 10 to 19; a moderate and severe depressive state, by a score ranging from 25 to 30 inclusively [44]. The French version of the GDS was validated using a Francophone population from New Brunswick and Québec [45] and the English version by Yesavage et al. [44]. The instrument has a test-retest reliability of 0.80 to 0.98 for a period ranging from one week to two months and of about 0.70 after six months [44,46].

Procedure

The research ethics approval for this study was obtained from the Comité d'éthique de la recherche avec les êtres humains from the Faculté des études supérieures et de la recherche (FÉSR) of the Université de Moncton. The geriatrician (or the doctor in charge) made the clinical diagnosis for MCI and AD and recruited participants for the project. The participants were first given a summary of the project and the phone number of a contact person. Then, they received clear explanation to the purpose of the project and the participation terms. Before their evaluation began, the consent form (for the participants and their legal guardians) was discussed with the participants (and their attendants) to ensure full understanding of the terms of participation. If the participants still wished to participate, they were asked (including their attendants) to sign the consent form.

The tests were administered at a single meeting in the presence of patient's proxy, whom provided corroborative information. The meetings lasted approximately 30 minutes. Control subjects were invited to participate in the study after attending presentation of the research project at various meetings of senior's associations and calls for participants at residences for independent and semi-independent persons. Individuals wishing to participate were asked to leave their contact information for follow-up. The meetings were held individually and voluntarily, using the same procedure as with the experimental group, except for the presence of an attendant, which was not mandatory. The exclusion criterion was based on the score obtained on the GDS, where a score above 25 on the GDS was used to exclude patients, due to the impact of severe depressive states on cognitive abilities. This led to the exclusion of three participants.

Analyses

The obtained data was scrutinized for the presence of outlier, normality and skewness. Descriptive statistics for the three groups was generated for each of the dependent variables as well as for the control variables (age, educational level, and the GDS score). Multivariate analysis of covariance (MANCOVA) using SPSS (IBM version 20) were calculated for each of the six dependent variables associated with executive functions and for the following independent variables, that is age, education, and GDS score. In order to see the effect of each covariables on the dependent variables and to better understand the underlying components of the targeted variables, standard multiple regressions analysis was run with the covariables acting as predictors. For multiple regressions, the effect-size, partial eta square (η^2) of the value 0.01 is considered as small, 0.06 as medium size, and 0.14 as large magnitude.

Results

The sample of participants was divided into three groups, i.e. the control group (CO), the MCI group and the AD group. For the

three groups, the descriptive statistics generated minimum and maximum values for each of the dependent variables as well as for the control variables, including age, educational level, and the score on the GDS. The means (M) for the whole set of variables studied are presented, by group in **Table 1**.

Table 2 shows the covariables effect on dependent variables using Pillai's criterion in the multivariate test; the combination of the dependent variables was significantly related to the whole set of covariables with a Pillai coefficient =0.81, to the education level with a Pillai coefficient =0.13, and to the GDS with a Pillai coefficient =0.13 but was non- significant with respect to age.

A link between the dependent variables and the whole set of covariables was demonstrated by η^2=0.41. The link between the dependent variables and the age covariable was however smaller in magnitude η^2=0.09, while reaching η^2=0.13 when associated with the education level and the scores on the GDS. The non-significant effect of the educational level on the majority of dependent variables (except for TMT B) was to be noted, contrary to expectations and the available literature on the subject. The level of education would therefore have little influence on the tests recommended in this study, i.e. within the sample examined.

Table 3 presents post-hoc analyses made using a Bonferroni correction (p=0.008) for multiple comparisons of the means for the groups under study for each dependent variable. Although the use of this criterion may increase the possibility of significant finding (making type II error), the fact that it reduces that of obtaining false positives (allowing individuals to obtain optimal treatment) justifies its use. A significant difference between the MCI group and the control group was especially sought as it is stipulated in this study's premise. As indicated in the literature review, the MMSE is not a powerful tool for detecting significant mean difference between the MCI and the control groups. The

Table 1 Descriptive statistics [mean and Standard deviation] of the groups (Total n = 116).

Variables	Control (*n* = 44)	MCI (*n* = 40)	AD (*n* = 32)
	M (SD)	***M (SD)***	***M (SD)***
Age Depressive symptoms	70.14 (7.21)	78.18 (7.83)	80.94 (7.72)
GDS Overall cognitive functions	2.39 (3.61)	9.45 (5.37)	9.60 (5.76)
MMSE Executive functions & visuo-constructive abilities	26.73 (2.56)	26.25 (2.73)	16.09 (3.82)
CLOC Executive functions	4.73 (0.62)	3.86 (1.23)	2.04 (1.37)
TMT-A	4.62 (2.32)	6.56 (3.08)	13.56 (4.68)
TMT-B	12.56 (7.65)	16.76 (8.59)	28.04 (3.66)
VFT-A	8.61 (3.56)	7.95 (4.39)	3.84 (3.00)
VFT-C	12.91 (4.44)	9.67 (2.90)	5.68 (2.95)

Note: AD: Alzheimer's Disease; CLOC: Clock Drawing; GDS: Geriatric Depression Scale; MCI: Mild Cognitive Impairment; M: Mean; MMSE: Mini Mental State Examination; SD: Standard deviation; TMT-A: Trail Making Test-A; TMT-B: Trail Making Test-B; VFT-A: Verbal Fluency Tests - Alphabetic; VFT-C: Verbal Fluency Tests - Category.

Table 2 Representation of the effect of the covariables on the respective dependent variables.

Covariables	Dependent Variables	Mean Square	F	Sig.	Partial Eta Square (η^2)	Observed Power
Age	MMSE[1]	1.26	0.14	0.71	0.00	0.07
	CLOC[2]	0.40	0.40	0.53	0.00	0.10
	TMTA[3]	1.89	0.22	0.64	0.00	0.08
	TMTB[4]	259.69	6.94	0.01*	0.06	0.74
	VFTA[5]	3.21	0.24	0.62	0.00	0.08
	VFTC[6]	53.74	4.43	0.04*	0.04	0.55
Education	MMSE	3.53	0.39	0.54	0.00	0.09
	CLOC	0.01	0.01	0.95	0.00	0.05
	TMTA	28.3	3.31	0.07	0.03	0.44
	TMTB	426.24	11.40	0.00*	0.09	0.92
	VFTA	49.79	3.75	0.06	0.03	0.48
	VFTC	16.66	1.37	0.24	0.01	0.21
GDS[7]	MMSE	9.30	1.01	0.32	0.01	0.17
	CLOC	6.4	6.35	0.01*	0.06	0.70
	TMTA	63.54	7.42	0.01*	0.06	0.77
	TMTB	264.31	7.07	0.01*	0.06	0.75
	VFTA	0.68	0.05	0.82	0.00	0.06
	VFTC	1.42	0.12	0.73	0.00	0.06

*p < 0.05; η^2 less than 0.06 = small; η^2 equal or higher than 0.06 = medium
[1]MMSE represents the Mini Mental State Examination.
[2]CLOC represents the Clock Drawing variable.
[3]TMTA represents the Trail Making Test part A.
[4]TMTB represents the Trail Making Test Part B.
[5]VFTA represents the Verbal Fluency Test - Alphabetic variable.
[6]VFTC represents the Verbal Fluency Test - Category variable.
[7]GDS represents the Geriatric Depression Scale variable.

same goes for the Verbal Fluency Test - Alphabetic (VFT-A). On tests of the Verbal Fluency Test - Category (VFT-C), the CLOC, the TMT- A and the TMT- B, a significant difference between groups (MCI and control) mean scores was observed, as shown in **Table 3**. This indicates that participants with MCI underperformed in comparison to the control group on cognitive tasks. This trend was also observed for the AD patients group, that AD group performed worst vis-a-vis other groups.

The result of the standard multiple regression analysis showed that no predictor had a significant impact on the Verbal Fluency Test - Alphabetic and the MMSE. The GDS significantly contributed to the scores on the CLOC, with the value of β being -0.05, which was significantly different from zero [*t* (109) =-2.52, *p*<0.05], just like this covariables' impact on the TMT A [β=0.15, *t* (109) =2.73, *p*<0.05]. Each of the identified predictors had a significant impact on the TMT B (*p*<0.05), [age β=0.21, *t* (109) = 2.64; education β=-3.33, *t* (109) =-3.38; GDS β=0.31, *t* (109) = 2.66]. Age was the only significant predictor of the scores on the *Verbal Fluency Test - Category* [β=-0.09, *t* (109) =-2.10, *p*<0.05].

Discussion and Conclusion

Our results are consistent with those from previous studies [17,21,47], indicating that executive functions incorporate several processes at a time, in spite of their distinct characteristics. The results have also demonstrated a significant difference for all the tests used among the three groups, except for the Verbal

Table 3 Comparison of means among the groups in relation to the dependent variables under study.

Dependent variable	Membership group	Marginal mean	Membership group	Mean difference	Standard error	Sig.
MMSE[1]	AD[2]	16.09	MCI	-10.16*	0.72	0.00
			Control	-10.63*	0.70	0.00
	MCI[3]	26.25	AD	10.16*	0.72	0.00
			Control	-0.48	0.66	1.00
	Control	26.73	AD	10.63*	0.70	0.00
			MCI	0.48	0.66	1.00
CLOC[4]	AD	2.03	MCI Control	-1.84* -2.69*	0.24 0.24	0.00 0.00
	MCI	3.87	AD	1.84*	0.24	0.00
			Control	-0.86*	0.22	0.00
	Control	4.73	AD	2.69*	0.24	0.00
			MCI	0.86*	0.22	0.00
TMTA[5]	AD	13.56	MCI	7.00*	0.73	0.00
			Control	8.94*	0.71	0.00
	MCI	6.56	AD	-7.00*	0.73	0.00
			Control	1.94*	0.67	0.01
	Control	4.62	AD	-8.94*	0.71	0.00
			MCI	-1.94*	0.67	0.01
TMTB[6]	AD	28.04	MCI	11.28*	1.65	0.00
			Control	15.48*	1.62	0.00
	MCI	16.76	AD	-11.28*	1.65	0.00
			Control	4.20*	1.52	0.02
	Control	12.56	AD	-15.48*	1.62	0.00
			MCI	-4.20*	1.52	0.02
VFTA[7]	AD	3.84	MCI Control	-4.11* -4.77*	0.87 0.86	0.00 0.00
	MCI	7.95	AD	4.11*	0.87	0.00
			Control	-0.67	0.80	1.00
	Control	8.61	AD MCI	4.77* 0.67	0.86 0.80	0.00 1.00
VFTC[8]	AD	5.68	MCI Control	-3.99* -7.23*	0.84 0.83	0.00 0.00
	MCI	9.67	AD	3.99*	0.84	0.00
			Control	-3.24*	0.78	0.00
	Control	12.91	AD	7.23*	0.83	0.00
			MCI	3.24*	0.78	0.00

*p <0.05
[1]MMSE represents the Mini Mental State Examination.
[2]AD represents the group with Alzheimer's disease.
[3]MCI represents the group with mild cognitive impairment.
[4]CLOC represents the Clock Drawing variable.
[5]TMTA represents the Trail Making Test part A.
[6]TMTB represents the Trail Making Test part B.
[7]VFTA represents the Verbal Fluency Test - Alphabetic variable.
[8]VFTC represents the Verbal Fluency Test - Category variable.

Fluency Test - Alphabetic (VFT-A), for which no significant result was noted between the MCI group and the control group. This result indicates the possibility that the MCI group was more severely affected at the semantic memory level than at the level of the executive functions, which would explain in part the non-significant difference between MCI and the control group on this measure. Further examination of the unique characteristics of the participants would be necessary in future studies to answer the questions emerging from the results of this study, since they are contrary to previous studies mentioned [14,48]. Also, the fact that MCI group consisted of individual with mixed domain of cognitive impairment, here may suggests that our MCI group potentially consisted of individuals with lesser executive dysfunction relative to semantic memory impairment; thus, the non-significant between group difference observed on executive functioning in relative to a significant result on semantic memory.

After dismissing the influence of the covariates on the dependent variables, significant differences among the means for the groups

were noticed. Particularly, a significant difference was observed with regards to the MCI group and the control group on their performance on the Clock Drawing Test, the TMT A and B and the Verbal Fluency Test - Category. A meta-analysis [48] supports this latter point by reporting that several studies have more or less obtained the same result.

The results also demonstrate that the executive function tasks used in addition to the screening tool, the MMSE, enabled us to clearly distinguish the difference between the average score of the AD group as opposed to the other two groups. In addition to converging towards results obtained by previous studies, these show once again that the scales used can be justified when seeking to differentiate between AD and MCI and when the symptomatology can be identified in the individual.

After studying the influence of the covariables on the dependent variables as a whole, some of them were not under the threshold of the significance level but were so close as to merit some attention. Although the TMT-A was significantly influenced only by the GDS, the education level's influence followed not far behind. The VFT-A was found to be in the same position, where the education level influenced its scores. The effect of this covariable on the other dependent variables is not negligible and the need to include it in future studies, or in tests on different samples, would allow for an update on its impact, real or not. The fact that these effects were underlined and described by the analyses discussed subscribes to the societal effort aimed at awareness and education with seniors [49]. The latter could be underprivileged, have a lower education level or manifest significant mood disturbances and still benefit from information on the subject.

Through simple tasks requiring the use of inhibition, mental flexibility and updating, the results of this project were able to confirm those of previous studies [17]. This allowed for the development of new exploration paths to put together a unique screening tool, simple and inexpensive in terms of time and money, to clearly distinguish the different clinical populations that could later be afflicted with Alzheimer type dementia. This study acted in an exploratory way to gather information about executive function tasks that could, in a subsequent study, be part of a battery of tests for the best possible detection of the prodromal dementia state.

In spite of the many precautions taken, this study had certain limits. Methodologically, equivalency could not be attained in the number of participants in the groups. The diagnostic procedures cannot be specified with respect to the MCI and AD groups, as they were not documented during the collection of the secondary data used in this project. This therefore limits the knowledge about the characteristics of the sample used, especially about the nature of the MCIs evaluated (amnesiac versus non-amnesiac), thereby restricting any generalization of the results obtained.

To refine the possible conclusions from the sample studied, it would be preferable, in a subsequent study, to adopt a more stringent exclusion criterion so as to discard any depressive symptom detected through the GDS, thus purifying the variance obtained. From a practical standpoint, these results are still very interesting as they are more representative of a typical elderly population in a clinical setting.

Furthermore, the homogeneity postulate of the variance-covariance matrices of the data studied was not respected, which in turn does not allow the basic postulates of the proposed analyses to be respected. It was also possible to identify a significant link between the covariables and the independent variable, i.e. age, as well as the score on the Geriatric Depression Scale, thus constituting another violation of the proposed analyses' basic postulate. Notwithstanding the violation of more than one postulate, the analyses were still considered and interpreted with precaution given the nature of the project's sample. The size of the sample may seem small when compared to similar studies [50,51].

In future research prospects lies the need to develop an efficient method for the early screening of Alzheimer's disease. For close to a decade now, executive functions have created a lot of interest by their simplicity and the attractiveness of their discriminatory efficiency for the different dementia states, from early to advanced stage. Following this study, it would be interesting to combine the tests with which it was possible to distinguish the groups studied to verify their discriminating power in a battery combining them. A comparison with more complex and pre-established neuropsychological test batteries within the medical community would help in determining its usefulness and appropriateness with the targeted population. It would in fact be interesting to subsequently verify the perceptions of health professionals, i.e. general practitioners and family doctors mostly, towards such a tool that would combine the functions studied here and that could ultimately lead to the early identification of AD.

Our results are in line with the recommendations made by Albert and colleagues [12] for the use of clinical criteria to simplify access to an assessment of cognitive functions and the diagnosis of AD. This could help foster early diagnosis and appropriate intervention and would certainly have positive implications at the social and fiscal level for the targeted individuals and families [52].

An additional interesting finding of our study is correlation between scores on CLOC and GDS that suggests the possible presence of depression of the executive dysfunction syndrome of late life within our sample. Depression-executive dysfunction syndrome [53-55] was described by Alexopoulos and colleague in early 2000s, as a distinct type of depression presenting in older adults with prominent executive functioning deficit. This finding warrants future studies investigating executive functioning in different aging groups (with and without pathology) with co-morbid depression of various types (e.g., AD+ depression by DSM–MDD criteria versus AD+depression of the executive type). By the same token, depression of AD that was suggested by the NIMH [56] and recently examined for validity [57] can be examined by the aforementioned hypothesis.

Our study is not without limitations, for example, as can be observed on **Table 3**, we have a large variation within groups on

Table 4 Representation of multiple regressions showing the influence of the covariables on the dependent variables individually.

Dependent variables	Covariables	*B*[1]	Standard error	*t*	Sig.	Confidence interval		Partial square eta	Observed power
						Inf.	Sup.		
MMSE[2]	Age	-0.02	0.04	-0.37	0.71	-0.09	0.06	0.00	0.07
	Education level	0.30	0.49	0.62	0.54	-0.67	1.27	0.00	0.09
	GDS[3]	-0.06	0.06	-1.01	0.32	-0.17	0.06	0.01	0.17
CLOC[4]	Age	-0.01	0.01	-0.63	0.53	-0.03	0.02	0.00	0.10
	Education level	-0.01	0.16	-0.07	0.95	-0.33	0.31	0.00	0.05
	GDS	-0.05	0.02	-2.52	0.01*	-0.09	-0.01	0.06	0.70
TMTA[5]	Age	0.02	0.04	0.47	0.64	-0.06	0.09	0.00	0.08
	Education level	-0.86	0.47	-1.82	0.07	-1.79	0.08	0.03	0.44
	GDS	0.15	0.06	2.73	0.01*	0.04	0.26	0.06	0.77
TMTB[6]	Age	0.21	0.08	2.64	0.01*	0.05	0.37	0.06	0.74
	Education level	-3.33	0.99	-3.38	0.00*	-5.29	-1.38	0.09	0.92
	GDS	0.31	0.12	2.66	0.01*	0.08	0.54	0.06	0.75
VFTA[7]	Age	-0.02	0.05	-0.49	0.62	-0.12	0.07	0.00	0.08
	Education level	1.14	0.59	1.94	0.06	-0.03	2.31	0.03	0.48
	GDS	-0.02	0.07	-0.23	0.82	-0.15	0.12	0.00	0.06
VFTC[8]	Age	-0.1	0.05	-2.10	0.04*	-0.18	-0.01	0.04	0.55
	Education level	0.66	0.56	1.17	0.24	-0.46	1.77	0.01	0.21
	GDS	0.02	0.07	0.34	0.73	-0.11	0.15	0.00	0.06

*p< 0.05
[1]Non-standardized coefficient.
[2]MMSE represents the Mini Mental State Examination.
[3]GDS represents the Geriatric Depression Scale variable.
[4]CLOC represents the Clock Drawing Test variable.
[5]TMTA represents the Trail Making Test part A.
[6]TMTB represents the Trail Making Test part B.
[7]VFTA represents the Verbal Fluency Test - Alphabetic variable.
[8]VFTC represents the Verbal Fluency Test - Category variable.

TMT-B, which is completely different from the rest of the scales scores. Thus, the heterogeneity in the variance observed across scales highlights variation in executive functioning across these patient groups. However, the variation is consistent within a scale, and that our result for the TMT-B is robust, as seen by the observed power, as presented in **Table 4**. On a different note, although a cutoff score to screen-out individuals with severe depressive mood was used, as per **Table 1**, it is noted that MCI and AD individuals meeting DSM-IV criteria cutoff score for major depression were included. Nonetheless, our executive functioning measures allowed differential diagnosis. In addition, in **Table 1**, group differences are obvious using MMSE scores, yet noteworthy that, this variation was used to screen patients into groups at onset. The present result warrants further examination of the executive functioning with these patients at a larger scale.

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References

1 Petersen RC, Morris JC (2005) Mild cognitive impairment as a clinical entity and treatment target. Arch Neurol 62: 1160-1163.

2 Reisberg B, Gauthier S (2008) Current evidence for subjective cognitive impairment (SCI) as the pre-mild cognitive impairment (MCI) stage of subsequently manifest Alzheimer's disease. Int Psychogeriatr 20: 1-16.

3 Jicha GA, Parisi JE, Dickson DW, Johnson K, Cha R, et al. (2006) Neuropathologic outcome of mild cognitive impairment following progression to clinical dementia. Arch Neurol 63: 674-681.

4 Saxton J, Lopez OL, Ratcliff G, Dulberg C, Fried LP, et al. (2004) Preclinical Alzheimer disease: neuropsychological test performance 1.5 to 8 years prior to onset. Neurology 63: 2341-2347.

5 Apostolova LG, Cummings JL (2008) Neuropsychiatric manifestations in mild cognitive impairment: a systematic review of the literature. Dement Geriatr Cogn Disord 25: 115-126.

6 Duarte LR, SyssauA, Jimenez M, Launay M, Terrier P (2007) Deficit of access or storage: semantic memory processing in Alzheimer disease. Can J Aging 26: 227-239.

7 Shankle WR, Romney AK, Hara J, Fortier D, Dick MB, et al. (2005) Methods to improve the detection of mild cognitive impairment. Proceedings of the National Academy of Sciences of the United States of America 102: 4919-4924.

8 Simard M, Hudon C, van Reekum R (2009) Psychological distress and risk for dementia. Curr Psychiatry Rep 11: 41-47.

9 Tierney MC, Yao C, Kiss A, McDowell I (2005) Neuropsychological tests accurately predict incident Alzheimer disease after 5 and 10 years. Neurol 64: 1853-1859.

10 Zhang Y, Han B, Verhaeghen P, Nilsson LG (2007) Executive functioning in older adults with mild cognitive impairment: MCI has effects on planning, but not on inhibition. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 14: 557-570.

11 Aggarwal NT, Wilson RS, Beck TL, Bienias JL, Bennett DA (2005) Mild cognitive impairment in different functional domains and incident Alzheimer's disease. J Neurol Neurosurg Psychiatry 76: 1479-1484.

12 Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, et al. (2011) The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease Alzheimers Dement 7: 270-279.

13 Backman L, Jones S, Berger AK, Laukka EJ, Small BJ (2005) Cognitive impairment in preclinical Alzheimer's disease: a meta-analysis. Neuropsychol 19: 520-531.

14 Baudic S, Barba GD, Thibaudet MC, Smagghe A, Remy P, et al. (2006). Executive function deficits in early Alzheimer's disease and their relations with episodic memory. Arch Clin Neuropsychol 21: 15-21.

15 Perry RJ, Hodges JR (1999) Attention and executive deficits in Alzheimer's disease: A critical review. Brain 122: 383-404.

16 Lafleche G, Albert MS (1995) Executive function deficits in mild Alzheimer's disease. Neuropsychol 9: 313.

17 Stuss DT, Alexander MP (2007) Is there a dysexecutive syndrome. Philos Trans R Soc Lond B Biol Sci 362: 901-915.

18 Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, et al. (2000) The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. Cogn Psychol 41: 49-100.

19 Blair C, Zelazo PD, Greenberg MT (2005) The measurement of executive function in early childhood. Dev Neuropsychol 28: 561-571.

20 Duncan J, Emslie H, Williams P, Johnson R, Freer C (1996) Intelligence and the frontal lobe: the organization of goal-directed behavior. Cogn Psychol 30: 257-303.

21 Miyake A, Friedman NP, Rettinger DA, Shah P, Hegarty M (2001) How Are Visuospatial Working Memory, Executive Functioning, and Spatial Abilities Related? A Latent-Variable Analysis. Journal of Experimental Psychology: General 130: 621-640.

22 Ismail Z, Rajji TK, Shulman KI (2010) Brief cognitive screening instruments: an update. Int J Geriatr Psychiatry 25: 111-120.

23 Brodaty H, Low LF, Gibson L, Burns K (2006) What is the best dementia screening instrument for general practitioners to use? Am J Geriatr Psychiatry 14: 391-400.

24 Lezak MD (2004) Neuropsychological assessment (4th vol). Oxford, New York, Oxford University Press.

25 Dikmen SS, Heaton RK, Grant I, Temkin NR (1999) Test-retest reliability and practice effects of expanded Halstead-Reitan Neuropsychological Test Battery. J Int Neuropsychol Soc 5: 346-356.

26 Cardebat D, Celsis P, Puel M, Doyon B, Viallard G (1991) Cerebral blood flow correlates of phonological and semantic verbal fluency performances in demented patients. J Neurolinguistics 6: 345-359.

27 Crawford JR, Henry JD (2005) Assessment of executive deficits. In PW Halligan & N Wade, The Effectiveness of Rehabilitation for Cognitive Deficits, London: Oxford University Press pp: 233-246.

28 Tombaugh TN (2004) Trail Making Test A and B: normative data stratified by age and education. Arch Clin Neuropsychol 19: 203-214.

29 Basso MR, Bornstein RA, Lang JM (1999) Practice effects on commonly used measures of executive function across twelve months. The Clinical Neuropsychologist 13: 283-292.

30 Jorm AF, Christensen H, Korten AE, Jacomb PA, Henderson AS (2001) Memory complaints as a precursor of memory impairment in older people: a longitudinal analysis over 7-8 years. Psychol Med 31: 441-449.

31 Godefroy O (2008) Fonctions exécutives et pathologies neurologiques et psychiatriques: Évaluation en pratique Clinique (1st Edn), p: 312.

32 Folstein MF, Folstein SE, McHugh PR (1975) "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research 12: 189-198.

33 Qizilbash N (2003) Evidence-based Dementia Practice. Oxford: UK, Blackwell Science Ltd.

34 Plake BS, Impara JC, Spies RA (2003) The Fifteenth Mental Measurements Yearbook. NE: Buros Institute of Mental Measurements.

35 Iverson GL (1998) Interpretation of Mini-Mental State Examination scores in community-dwelling elderly and geriatric neuropsychiatry patients. Int J Geriatr Psychiatry 13: 661-666.

36 Tombaugh TN, McIntyre NJ (1992) The Mini-Mental State Examination: a comprehensive review. J Am Geriatr Soc 40: 922-935.

37 Reitan RM (1958) Validity of the Trail Making Test as an indicator of organic brain damage. Perceptual and Motor Skills 8: 271-276.

38 Amieva H, Goff ML, Stoykova R, Lafont S, Ritchie K, et al. (2009) Trail Making Test A et B (version sans correction des erreurs): normes en population chez des sujets âgés, issues de l'étude des trois Cités. Revue de neuropsychologie 1: 210.

39 Gladsjo JA, Schuman CC, Evans JD, Peavy GM, Miller SW, et al. (1999) Norms for letter and category fluency: demographic corrections for age, education, and ethnicity. Assessment 6: 147-178.

40 Tombaugh TN, Kozak J, Rees L (1999) Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. Arch Clin Neuropsychol 14: 167-177.

41 Freedman M (1994) Clock drawing: a neuropsychological analysis. New York: Oxford University Press.

42 Shulman KI (2000) Clock-drawing: is it the ideal cognitive screening test? International J Geriatric Psychiatry 15: 548-561.

43 Ruchinskas RA, Curyto KJ (2003) Cognitive screening in geriatric rehabilitation. Rehabilitation Psychol 48: 14-22.

44 Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, et al. (1983) Development and validation of a geriatric depression screening scale: a preliminary report. J Psy Res 17: 37-49.

45 Bourque P, Blanchard L, Vézina J (1990) Étude psychométrique de l'Échelle de dépression gériatrique, Canadian Journal on Aging / La Revue canadienne du vieillissement 9: 348-355.

46 Ingraham F (1996) The short geriatric depression scale. Clin Gerontol 16: 49-56.

47 Godefroy O, Cabaret M, Petit-Chenal V, Pruvo JP, Rousseaux M

(1999) Control functions of the frontal lobes. Modularity of the central-supervisory system? Cortex 35: 1-20.

48 Henry JD, Crawford JR, Phillips LH (2004) Verbal fluency performance in dementia of the Alzheimer's type: a meta-analysis. Neuropsychol 42: 1212-1222.

49 World Health Organization (2013) Mental Health Action Plan.

50 Albert MS, Moss MB, Tanzi R, Jones K (2001) Preclinical prediction of AD using neuropsychological tests. J Int Neuropsychol Soc 7: 631-639.

51 Bozoki A, Giordani B, Heidebrink JL, Berent S, Foster NL (2001) Mild cognitive impairments predict dementia in nondemented elderly patients with memory loss. Arch Neurol 58: 411-416.

52 Weimer DL, Sager MA (2009) Early identification and treatment of Alzheimer's disease: social and fiscal outcomes. Alzheimers Dement 5: 215-226.

53 Alexopoulos GS (2001) "The depression-executive dysfunction syndrome of late life": a specific target for D3 agonists? Am J Geriatr Psychiatry 9: 22-29.

54 Alexopoulos GS, Kiosses DN, Klimstra S, Kalayam B, Bruce ML (2002) Clinical presentation of the depression-executive dysfunction syndrome of late life. Am J Geriatr Psychiatry 10: 98-106.

55 Alexopoulos GS, Meyers BS, Young RC, Kalayam B, Kakuma T, et al. (2000) Executive dysfunction and long-term outcomes of geriatric depression. Arch Gen Psychiatry 57: 285-290.

56 Olin JT, Schneider LS, Katz IR, Meyers BS, Alexopoulos GS, et al. (2003) Provisional diagnostic criteria for depression of Alzheimer's disease: description and review. Expert Rev Neurother 3: 99-106.

57 Sepehry AA, Lee PE, Hsiung GR, Beattie BL, Feldman HH, et al. (2017) The 2002 NIMH provisional diagnostic criteria for depression of Alzheimer's disease (PDC-dAD): Gauging their validity over a decade later. J Alzheimers Dis 58: 449-462.