Clinical Utility of the Envelope Task in Mild Cognitive Impairment and Dementia

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ABSTRACT: *Objective*: Prospective memory (PM) is a cognitive function defined as the ability to perform an intention at an appropriate moment in the future. In the aging population, PM is essential for maintaining independent daily living. Introduced as a simple and quick way to assess PM in clinical settings, the envelope task has to date received very limited empirical and practical interest. *Methods*: The present study investigated the task's clinical utility in detecting PM impairment in a sample composed of 49 healthy older adults (OA), 41 patients with Alzheimer's disease, and 64 individuals with amnestic and nonamnestic mild cognitive impairment (MCI) of heterogeneous etiology: 17 of idiopathic nature, 20 presenting an idiopathic rapid-eye movement sleep behaviour disorder, and 27 patients diagnosed with idiopathic Parkinson's disease. *Results*: The envelope task was highly sensitive and specific in discriminating Alzheimer's disease patients from OA. Although it was specific in distinguishing MCI individuals from OA, its sensitivity was modest, especially in patients presenting a nonamnestic MCI subtype. *Conclusions*: Given its high specificity and simple low-cost administration procedure, the envelope task is a promising instrument for clinicians who seek to rapidly assess PM impairment in their daily practice.

RÉSUMÉ: *Contexte:* La mémoire prospective (MP) est une fonction cognitive qui se définit par la capacité à effectuer une action à un moment préalablement déterminé dans le futur. La MP joue un rôle crucial chez les personnes âgées dans le maintien de leur indépendance fonctionnelle dans la vie quotidienne. Parmi les mesures de PM décrites dans la littérature, la tâche de l'enveloppe est une épreuve simple et rapide à administrer, mais pourtant rarement utilisée par les chercheurs et les cliniciens. *Méthodologie:* L'objectif de la présente étude était d'investiguer l'utilité clinique de cette épreuve dans la détection de troubles de la MP auprès d'un échantillon composé de 49 sujets sains, 41 patients atteints de la maladie d'Alzheimer et 64 individus ayant un trouble cognitif léger (MCI) amnésique ou non-amnésique d'étiologies hétérogènes: 17 de nature idiopathique, 20 présentant un trouble comportemental en sommeil paradoxal et 27 atteints de la maladie de Parkinson. *Résultats:* La tâche de l'enveloppe s'est avérée très sensible et spécifique pour discriminer les patients atteints d'une maladie d'Alzheimer des sujets sains. Sa spécificité était bonne pour discriminer les MCI des sujets sains, mais la tâche de l'enveloppe demeurait peu sensible chez les MCI surtout chez les MCI non-amnésiques. *Conclusion:* En raison d'une grande spécificité et de la facilité d'administration, la tâche de l'enveloppe est donc une mesure intéressante pour tout de clinicien désirant rapidement évaluer la MP dans leur pratique.

Reminding oneself to pick up clothes at the dry cleaner's after work or to take a pill before bedtime are but some of the many examples used to illustrate the role of prospective memory (PM) in daily life. The ability to remember to execute an intended action in the future is dependent on two distinct features: a prospective component (PC) and a retrospective component (RC). Although the first generates the thought of a planned intention to be performed, alerting one to detect the appropriate moment of execution, the second provokes a recall of the intention's content to perform it correctly.[1,2] Unlike the memory of past events, formally known as retrospective episodic memory, PM requires a self-initiated retrieval of information. Typical PM paradigms require an intended action to be (1) embedded in an ongoing activity and (2) executed at a precise, delayed, and predetermined event- or time-based occasion.[3] PM processing thus includes a sequence of phases: (1) recording the intention (e.g. memorizing the contents and cues associated to the intention, planning and strategizing how to detect cues accurately), (2) storing

the intention in memory, (3) once the adequate moment (time-based) or cue (event-based) is detected in the environment, interrupting the ongoing activity to immediately execute the intention according to the initial plan, and (4) verifying and deleting the intention from one's mind.[4-6] From a neuroanatomical perspective,

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there is evidence suggesting that distinct cerebral networks mediate each PM component. Processes relating to the RC seem to require similar hippocampal structures implicated in episodic memory,[1,7-9] whereas those responsible for the PC are shown to rely on prefrontal structures of the brain,[10-14] known to occupy a crucial role in attention and executive functions.[15,16]

In neuropsychology, there has been an overwhelming interest in defining retrospective memory deficits in preclinical and clinical stages of dementia. In contrast, few studies have investigated the prognostic value of PM deficits despite subjective complaints from patients diagnosed with Alzheimer's disease (AD) and their caregivers.[17] So far, PM impairment has been objectively detected in AD when compared with controls, characterized by difficulties on the PC and the RC.[18,19] A similar pattern was observed even in patients with mild dementia, suggesting that a decline in PM performance could serve as a marker for early-stage AD.[20-22] Significant PM deficits have also been reported in individuals with mild cognitive impairment (MCI), an intermediate state between normal cognitive functioning and dementia.[19,23-28]

Given its essential role in maintaining independent daily living, it would be wise to evaluate PM at a more systematic rate, especially in the aging population. Several standardized PM measures have been developed over the years. The envelope task[29] is of particular interest because of its ability to assess PM components individually using a simple and rapid procedure. Since its first mention in the literature, this task has unfortunately spiked very little practical and empirical interest despite the fact that it has been reported to be particularly sensitive to early stages of dementia. To our knowledge, only two studies[30,31] have assessed PM using the envelope task and only one of these[30] has investigated its diagnostic properties in amnestic MCI (aMCI). To date, there is no published report on the envelope task's clinical value among patients with nonamnestic MCI (naMCI).

The primary purpose of the present study was to observe the performance on the envelope task across different cognitive profiles in preclinical and clinical phases of dementia (AD, aMCI, and naMCI) and to characterize the relative nature of PM deficits (PC and/or RC). We expected AD patients to perform poorly on both PM components and MCI patients to show milder yet significant PM impairment in relation to the subtype: aMCI to perform poorly only on the RC (given their predominant memory deficits) and naMCI to perform poorly only on the PC (given their predominant deficits in cognitive domains other than memory). As a secondary purpose, we sought to investigate the diagnostic utility of the envelope task (sensitivity and specificity). In the hopes that it would be an excellent PM measure in clinical settings, this task was expected to exhibit high sensitive and specific screening qualities among individuals with MCI and AD.

METHODS

Participants

The present study received full ethical approval. Subjects were recruited from various health care facilities (Hôpital Notre-Dame of the Centre Hospitalier de l'Université de Montréal, Center for Advanced Research in Sleep Medicine of the Hôpital du Sacré-Coeur de Montréal, Department of Neurology of the Montreal General Hospital, Centre de recherche de l'Institut universitaire de gériatrie de Montréal) and gave written informed consent before participating in the study. All participants underwent a standard neurological and neuropsychological assessment without interrupting any medication regimens. Neuropsychological tests measuring various cognitive domains, such as executive functions, attention, memory, language, visuoconstructional, and visuoperceptual skills, were administered and scored according to standard procedure.[32,33] Based on the results of their clinical examination, subjects were then selected and designated to a clinical group.

The AD group included 41 patients with mild dementia (Mini-Mental State Examination [MMSE] scores ≥20). Probable AD diagnosis was made by a neurologist or a geriatrician following the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria.[34] Laboratory tests (e.g. computed tomography scan, single-photon emission computed tomography and/or magnetic resonance imaging, urinalysis) were also performed to rule out any viral, metabolic, or traumatic causes of dementia.

The MCI group consisted of 64 individuals diagnosed according to Petersen's criteria:[35] (1) subjective complaint or concern regarding cognitive function expressed by the patient or a reliable informant; (2) objective evidence of cognitive decline defined as a performance of ≥1.5 standard deviations below the standardized mean on at least two variables in a single cognitive domain; (3) general preservation in functional activities of daily living; (4) absence of any clinical signs suggesting the presence of dementia; and (5) absence of medication or other medical/psychiatric disorders that may better explain the observed cognitive decline. Note that this sample was heterogeneous: 17 individuals presented an idiopathic form of MCI (absence of any associated medical condition), whereas the other 47 individuals were diagnosed with a prior medical condition (concomitant MCI) such as idiopathic Parkinson's disease (PD; n = 27) or idiopathic rapid eye movement sleep behavior disorder (iRBD; n = 20), a parasomnia characterized by violent dream-enacting sleep behavior. According to recent reports, approximately one-third of PD patients[36-38] and one-half of iRBD patients[39] are concomitantly diagnosed with MCI, which may increase their risk of developing dementia in later years.[40-42] Moreover, PD and iRBD patients were included in this study given their high prevalence for naMCI subtype.[39] Based on their overall neuropsychological performance, MCI patients were further categorized into amnestic and nonamnestic subgroups. The aMCI group included 15 single-domain (predominant and isolated memory impairment) and 24 multiple-domain participants (secondary impairment in executive functioning), whereas the naMCI group included 21 single-domain (predominant and isolated impairment in executive functioning) and four multiple-domain participants (secondary impairment in memory and visuospatial capacities). Finally, 49 healthy older adults (OA) were also included in this study and served as a control comparison group.

All participants were between 50 and 89 years of age, francophone or bilingual, and had completed at least 4 years of formal education. Exclusion criteria included: (1) antecedent disease of the central nervous system except for AD, PD, or iRBD (e.g. cerebrovascular accident, traumatic brain injury, epilepsy);

(2) presence of an associated severe disease except for AD, PD, or iRBD (e.g. diabetes, kidney insufficiency); (3) presence of psychiatric disease (e.g. schizophrenia, depression); (4) antecedent substance abuse (e.g. alcohol, illicit and/or prescription drugs); (5) antecedent diagnosed learning disorders (e.g. dyslexia, attention deficit hyperactivity disorder) or important sensory deficits susceptible to impairing the neurological and neuropsychological evaluation.

PM Assessment

To evaluate PM, the envelope task[29] was included in the neuropsychological assessment. Following the suggested procedure, this event-based, single-trial PM task involved instructing the participant to write a dictated name and address onto an envelope and to spontaneously perform two actions thereafter: (1) to seal and (2) to write their own initials along the envelope's flap. Once the participant confirmed having clearly understood these instructions, the evaluator proceeded in administrating various other cognitive tasks included in the standardized neuropsychological battery. After a 10-minute delay, the evaluator provided the participant with a blank envelope and dictated, at a reasonable pace, a fictional name and address. Upon writing the address, the evaluator then quietly observed if the subject would spontaneously execute the two intended actions (to seal and to write their initials along the envelope's flap) as previously instructed. If no response was initiated within a few seconds, the evaluator openly questioned the participant if something else involving the envelope needed to be carried out. Following Einstein and McDaniel's theory, this task can individually assess PC and RC performance. Points on the PC were given if the participant spontaneously executed both or either one of the two intended actions (envelope sealed and/or initials written at the back), scored as 2 or 1, respectively. If the participant failed to spontaneously perform one or both actions (PC score = 0 or 1), points were distributed according to the participant's ability to remember the content of each action upon prompting (RC): 2 points for recalling both intentions, 1 point for recalling either one of the intentions, or 0 points if unable to recall any of the intentions. This informed the evaluator if prompting was beneficial for the participant in retrieving the intentions. According to Huppert et al's[29] previously described scoring instructions, the performance of each PM component was then dichotomized. On the PC, performance was defined as successful if the subject executed at least one (PC score = 1) or both (PC score = 2) of the intentions without a prompt, and unsuccessful if the subject failed to respond without a prompt (PC score = 0). On the RC, performance was defined as successful if the subject strictly remembered, with or without prompt, the contents of both intentions (RC score = 2) and unsuccessful if the subject forgot the contents of one (RC score = 1) or both (RC score = 0) intentions.

Statistical Analysis

Raw data were imported into version 21 of the Statistical Package for the Social Sciences software and underwent preliminary analyses to ensure that all outcome variables were distributed normally. One-way analyses of variance were computed to compare mean differences between OA, aMCI, naMCI, and AD groups on demographic characteristics, followed by post hoc

tests using Hochberg's GT2 (unequal sample sizes) or Games-Howell (homogeneity of variance not respected) procedures when necessary. Regarding data collected from the neuropsychological assessment, raw scores for each test were converted to demographically adjusted Z scores, then grouped according to their respective cognitive domain, selected on an a priori conceptual basis, and finally averaged to generate two distinct composite measures of cognitive functioning. Specifically, episodic memory included the following measures: (1) Rey Auditory Verbal Learning Tests (sum of trials 1 through 5 and delayed recall) or (2) Buschke 16-item Free and Cued Selective Reminding Test (sum of free recall trials 1 through 3 and delayed free recall). Measures used to represent executive functioning were: (1) Trail Making Test, part B – part A (time); (2) Trail Making Test, part B (errors); (3) semantic verbal fluency; and (4) phonetic verbal fluency. Planned one-way analyses of variance and correlations were performed using these two composite measures.

Because dichotomized PC and RC scores yielded ceiling and floor effects, contingency tables, χ^2, and Fisher exact test of independence (for small expected frequencies) tests were performed to compare proportions of patients that succeeded or failed on each PM component of the task. Using Cohen's criteria,[43] effect sizes were determined using the phi coefficient (φ) for 2 × 2 contingency tables or Cramer's V (φ_c) for larger than 2 × 2 contingency tables. Pearson correlations were also computed to investigate the possible relation between dichotomized PM performance and cognitive functioning (memory and executive functions composite scores).

Finally, receiver operating characteristic (ROC) curves (area under the curves [AUC; 95% confidence interval, CI]) were computed to determine if the envelope task could be an effective screening tool in detecting PM deficits among aMCI, naMCI, and AD. Using PC and RC scores, the task's sensitivity, specificity, positive predicted value, negative predicted value, and Youden Index were examined. Statistical significance was set at $p < 0.05$.

RESULTS

Demographic, clinical, and cognitive characteristics

Demographic and clinical characteristics of all 154 participants included in this study are presented in Table 1. Groups significantly differed in age (F [3,150] = 21.39; $p < 0.05$), education (F [3,150] = 6.20; $p < 0.05$), and MMSE performance (F [3,150] = 23.32; $p < 0.05$). Post-hoc comparisons revealed that OA and AD were among the oldest and less educated participants of the total sample. Furthermore, a gradual gradient of cognitive impairment was observed across groups according to MMSE performance: OA as the most cognitively intact followed by aMCI and naMCI (performed similarly), and finally AD as the most cognitively impaired. Chi-square analyses revealed significant gender differences between groups: χ^2 (3) = 20.56, $p < 0.001$, φ_c = 0.365. There was a higher proportion of men among aMCI and naMCI groups whereas a higher proportion of women in AD and OA groups.

Significant group differences were noted on composite measures of episodic memory (F [3,150] = 99.15; $p < 0.001$) and executive functions (F [3,144] = 18.24; $p < 0.001$) (Table 2). Episodic memory measures were significantly lower in patients with AD followed by those with aMCI in comparison to naMCI

Table 1: Participant demographic and clinical characteristics

	OA n = 49	aMCI n = 39	naMCI n = 25	AD n = 41	
Characteristics	**A**	**B**	**C**	**D**	*p*
iMCI, n (%)	–	15 (88)	2 (12)	–	–
iRBD, n (%)	–	8 (40)	12 (60)	–	–
PD, n (%)	–	16 (59)	11 (41)	–	–
Single domain, n (%)	–	15 (38)	21 (84)	–	–
Multiple domain, n (%)	–	24 (62)	4 (16)	–	–
Sex, female/male[a]	32/17	15/24	8/17	32/9	<0.001
Age, years	76.9 ± 7.2	71.1 ± 8.0	66.7 ± 7.6	80.0 ± 6.4	<0.001; A > B, A > C, D > B, D > C
Education, years	11.3 ± 4.3	14.4 ± 4.6	12.9 ± 3.9	10.7 ± 4.1	0.001; B > A, B > D
MMSE	29.1 ± 1.1	27.6 ± 2.2	28.3 ± 1.5	25.7 ± 2.4	<0.001; A > B > D, A > C > D

OA, older adults; aMCI, amnestic mild cognitive impairment; naMCI, non amnestic mild cognitive impairment; AD, Alzheimer's disease; iMCI, idiopathic mild cognitive impairment; iRBD, idiopathic REM sleep behavior disorder; PD, Parkinson's disease; MMSE, Mini Mental State Examination.
Proportion of participants is in parentheses.
Results are expressed as mean ± standard deviation.
[a]χ^2 analyses.

Table 2: Cognitive performance on neuropsychological assessment

	OA n = 49	aMCI n = 39	naMCI n = 25	AD n = 41	
Composite scores	**A**	**B**	**C**	**D**	p
Episodic memory	0.05 ± 1.16	−1.83 ± 1.06	0.27 ± 1.02	−3.67 ± 1.31	<0.001; D < B < A, B < C, D < C
Executive functions	0.17 ± 0.59	−0.72 ± 1.35	−1.18 ± 0.80	−1.05 ± 0.76	<0.001; C < A, B < A, D < A

OA, older adults; aMCI, amnestic mild cognitive impairment; naMCI, non amnestic mild cognitive impairment; AD, Alzheimer's disease.
Results represent the mean ± standard deviation of z scores.

patients and OA whose performance rated similarly. In comparison to healthy controls, all patients performed poorly on tests of executive functions. Although patients with naMCI showed the most difficulty, their performance was not statistically different from that of other patient groups (AD and aMCI).

Prospective Memory Performance

For clinical purposes, the distribution of nondichotomized PM performance is presented in Figure 1. The following results are however based on dichotomized PM performance. When comparing among OA, AD, and MCI (aMCI and naMCI combined) groups, a significant difference was noted on the PC (χ^2 [2] = 68.26, p < 0.001, $\varphi_c = 0.67$) and on the RC response rate (χ^2 [2] = 74.60, p < 0.001, $\varphi_c = 0.70$). As expected, OA outperformed patients with MCI and AD. As shown in Figure 1, nearly all controls successfully performed the task: most (85.7%) spontaneously executed both intentions while 14.3% executed only one of the intentions (PC). After prompting (RC), all but one among the latter remembered to execute the other forgotten intention.

MCI participants scored significantly lower compared with OA on the PC (χ^2 [1] = 8.40, p < 0.05, $\varphi = -0.27$) and on the RC (χ^2 [1] = 10.45, p < 0.05, $\varphi = -0.30$). Additional analyses revealed that, as opposed to controls, aMCI individuals performed significantly lower on both components (PC [χ^2 (1) = 12.60, p < 0.001, $\varphi = -.038$]; RC [χ^2 (1) = 12.62, p < 0.001, $\varphi = -0.38$]). The majority (76.9%) spontaneously performed one (23.1%) or both (53.8%) intentions, whereas nearly one-quarter of aMCI
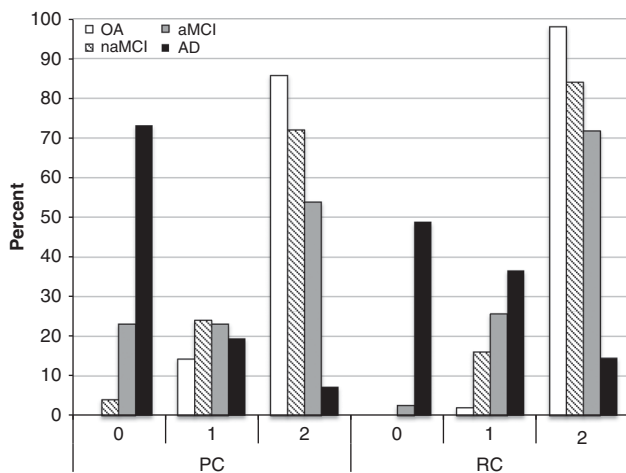
Figure 1: Performance on the envelope task. Nondichotomized scores on the prospective and retrospective components of the envelope task. OA, older adults; aMCI, amnestic mild cognitive impairment; naMCI, non amnestic mild cognitive impairment; AD, Alzheimer's disease; PC, prospective component; RC, retrospective component.

subjects (23.1%) failed to respond altogether. Prompting was helpful for most (71.8%), whereas others (28.2%) either responded incompletely (25.6%) or still failed to respond (2.6%). Compared with OA, naMCI individuals performed significantly lower solely on the RC (χ^2 [1] = 5.12, p < 0.05, φ = −0.26) but not on the PC (χ^2 [1] = 1.99, p > 0.05, φ = −0.16). Only 4% of naMCI individuals failed to spontaneously execute at least one of the intended actions (96% successfully performed the PC). Prompting proved beneficial to 84% of the group, whereas 16% still showed difficulty in retrieving one of the intentions. PM performance also varied within the MCI sample. Overall, individuals with a nonamnestic subtype scored higher on the envelope task than those with an amnestic subtype. These groups only differed significantly on the PC (χ^2 [1] = 4.21, p < 0.05, φ = −0.26) but not on the RC (χ^2 [1] = 1.27, p = 0.26, φ = −0.14).

AD patients performed significantly worse than OA on the PC (χ^2 [1] = 53.78, p < 0.001, φ = −0.77) and on the RC (χ^2 [1] = 64.58, p < 0.001, φ = −0.85). The same pattern of results was observed when comparing AD and MCI groups (aMCI and naMCI combined) on the PC (χ^2 [1] = 35.09, p < 0.001, φ = −0.58) and the RC (χ^2 [1] = 38.42, p < 0.001, φ = −0.61). The majority of AD participants (73.2%) failed to spontaneously perform any of the intended actions (PC). Prompting seemed somewhat beneficial, as some were able to remember one (36.6%) or both intentions (14.6%). However, almost half (48.8%) of AD participants were unresponsive to prompts. For further investigation, we divided the MCI group in subtypes to compare results with the AD group. There were significant differences on both PM components equally observed in the aMCI sample (PC [χ^2 (1) = 20.08, p < 0.001, φ = −0.50]; RC [χ^2 (1) = 26.72, p < 0.001, φ = −0.58]) as well as in the naMCI sample (PC [χ^2 (1) = 29.83, p < 0.001, φ = −0.67]; RC [χ^2 (1) = 30.91, p < 0.001, φ = −0.68]).

Further, large correlations were observed between the episodic memory composite measure and dichotomized RC and PC performances, r = 0.55, n = 154, p < 0.001 and r = 0.61, n = 154, p < 0.001, respectively. This indicates that a better performance on standardized episodic memory tests is associated to a greater success rate on each PM component. Although significant, weaker correlations were yielded between the executive function composite measures and dichotomized PC (r = 0.20, n = 148, p < 0.05) and RC (r = 0.18, n = 148, p < 0.05) performances.

Sensitivity and specificity

Results from ROC curve analyses are presented in Table 3. When examining performance between OA and AD, both the PC and the RC yielded significant AUCs of 0.94 (95% CI, 0.89-1.00, p < 0.001) and 0.92 (95% CI, 0.86-0.99, *p* < .001), respectively. The optimal cutoff values, providing the greatest accuracy for differentiating between OA and AD individuals, was 0 for the PC (0 indicates impairment, 73% sensitivity, 100% specificity) and ≤1 for the RC (0 or 1 indicates impairment, 85% sensitivity, 98% specificity), which corresponds to the criterion used by Huppert et al's[29] original study. ROC curves analyses between OA and aMCI participants also yielded significant AUCs for the PC (0.68; 95% CI, 0.56-0.79; p < 0.05) and the RC (0.63; 95% CI, 0.51-0.75, p < 0.05). However, using the same cutoff values mentioned previously decreased the sensitivity on the PC (23%) and the RC (28%) while still maintaining high specificity (100% for PC and 98% for RC). In contrast, ROC curve analysis was

Table 3: Summary of ROC analyses with cutoff scores

Group comparison	OA vs AD		OA vs aMCI		OA vs naMCI	
Prospective component						
Cutoff	0/2	≤1/2	0/2	≤1/2	0/2	≤1/2
Sensitivity, %	73	93	23	46	4	28
Specificity, %	100	86	100	86	100	86
PPV, %	100	84	100	72	100	50
NPV, %	82	93	62	67	23	70
Accuracy value	0.73	0.78	0.23	0.32	0.04	0.14
AUC (95% CI)	0.94** (0.89-1.00)		0.68* (0.56-0.79)		0.57 (0.43-0.71)	
Retrospective component						
Cutoff	0/2	≤1/2	0/2	≤1/2	0/2	≤1/2
Sensitivity, %	49	85	3	28	0	16
Specificity, %	100	98	100	98	100	98
PPV, %	100	97	100	92	NA	80
NPV, %	70	89	56	63	66	70
Accuracy value	0.49	0.83	0.03	0.26	0	0.14
AUC (95% CI)	0.92** (0.86-0.99)		0.63* (0.51-0.75)		0.57 (0.43-0.71)	

PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve; OA, healthy older adults; aMCI, amnestic Mild Cognitive Impairment; naMCI, non amnestic Mild Cognitive Impairment; AD, Alzheimer's disease.
Accuracy value is according to the Youden Index. Values in parentheses denote 95% CI.
*Significant value (p < 0.05).
**Significant value (p < 0.001).

not significant between OA and naMCI, with an AUC of 0.57 for the PC as well for the RC (95% CI, 0.43-0.71; p > 0.05).

DISCUSSION

The primary objective of the current study was to assess the possible PM impairment throughout preclinical and clinical phases of dementia using a simple clinical task. As expected, AD patients had significant difficulty performing the envelope task compared with other groups, including healthy older adults whose performance was nearly flawless. In fact, not only did the majority (73.2%) of AD patients fail to spontaneously execute both intentions (PC), but nearly half (48.8%) couldn't retrieve the content of either intention once prompted (RC). In other words, 26.8% (100% - 73.2%) of AD patients performed the task successfully (PC score of 1 or 2). In a previous report,[29] only 8% of individuals with probable dementia successfully performed the envelope task. Contrasting results between our study and the latter may be explained by the use of different AD diagnostic criteria. Schaub, Linden, and Copeland[44] suggest that the Diagnostic and Statistical Manual of Mental Disorders diagnoses a higher proportion of dementia cases than semistructured interviews, like the one used by the compared to study (e.g., Automated Geriatric Examination for Computer Assisted Taxonomy). In light of this evidence, it is possible that the results reported in Huppert et al[29] are underestimated given their use of a less reliable AD diagnostic protocol as opposed to ours, which is known to be compatible

with the Diagnostic and Statistical Manual of Mental Disorders (e.g. National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association). The higher success rate observed in our AD sample may also be due to the fact that, unlike the previous study, participants did not perform intentions in the context of another memory test (i.e. remembering the name and address of the envelope task), thus rendering the task simpler and less cognitively demanding. Nevertheless, our results are consistent with the only available previous report indicating the presence of a generalized PM impairment on the envelope task in mildly demented AD[29] and can be added to the existing literature on PM deficits in AD assessed by other measures.[20,21,25,29,45-50]

MCI patients demonstrated a less severe PM impairment as opposed to AD counterparts; however, our prediction that the former's struggle with the envelope task would be relative to their subtype was disproved. Instead of finding an isolated impairment on the RC, difficulties observed in aMCI were broader in nature, characterized by significant trouble in spontaneously executing (PC) *and* retrieving (RC) the intentions of the task. Regarding naMCI, impairment was indeed observed on an isolated PM component, but results pointed to an RC deficit rather than a predicted PC deficit. In sum, our results indicate that the performance on a single PM component (PC) significantly differentiates MCI groups. Neuropsychological profiling offers some aid in explaining the aforementioned discrepancies. Contrary to our assumptions, episodic memory was the only cognitive domain (of the two that were evaluated) that significantly distinguished aMCI from naMCI patients. Comparable executive functioning in both groups may be attributed to sample bias: more than half of the aMCI sample (62%) was composed of patients presenting a multiple-domain subtype (secondary impairment in executive functioning) and the majority of the naMCI sample (84%) presented a single-domain dysexecutive subtype. In this regard, it appears logical that aMCI patients performed poorly on both PM components because of a simultaneous decline in memory and executive functions. It remains puzzling however that (1) naMCI patients struggled only on the RC, when neuropsychological testing confirmed a relative preservation of their memory capacities (comparable to OA) and that (2) aMCI and naMCI groups differed only on the PC despite showing comparable performance on standardized executive function tests. Underlying factors could therefore be contributing to the observed PM impairment. According to our correlational analyses, the prospective and retrospective components of the envelope task were more strongly associated to the episodic memory composite measure, which leads us to consider that this test might be mainly relying on mnemonic functions. In retrospect, it is conceivable that the cognitive load would be greater on retaining the content of the intentions than on detecting the appropriate moment to execute them, because the evaluator exercises a certain control over the latter. In fact, handing the participant a blank envelope doesn't truly challenge that participant to spontaneously disrupt an ongoing activity (i.e. neuropsychological assessment) and also acts as a cue in itself to perform intentions afterwards. Given that the performance on the task seems to evaluate more certainly one's ability to store and remember the intentions, it is therefore not surprising that patients with limited memory resources (AD and aMCI) were more vulnerable to the task's demands than individuals whose memory capacities were globally intact

(naMCI and OA). In fact, even though differences on the RC between MCI groups did not reach significance, prompting seemed a lot more beneficial to individuals with naMCI than those with aMCI. Nonetheless, that a minor portion of naMCI subjects (16%) showed some degree of forgetfulness shouldn't be ignored. One can postulate that this represents a subset of naMCI patients presenting lower performance on episodic memory measures than others. Last, significant correlations between executive functioning and performances on the PC and the RC are not to be ignored; however, we caution interpretation because of the weakness of the observed slopes. Further studies are needed to explore the underlining mechanisms possibly attributing to PM difficulties seen in naMCI.

Results regarding aMCI in particular contrasted with those of a recent study,[30] which reported aMCI subjects as showing more difficulty on the RC rather than on the PC of the envelope task. A few reasons may explain these inconsistent findings. First, a different scoring procedure was adopted than the one originally used by Huppert et al:[29] PC performance not only strictly considered as the spontaneous detection of the appropriate moment to perform the intention but also as the response produced by prompting, thus elevating the PC scores obtained in Delprado et al's aMCI sample.[30] Second, because of a very high frequency of ceiling and floor effects within our study's sample, we performed χ^2 tests instead of conventional parametric tests, which might be less sensitive to subtle groups differences. Finally, although the aMCI global cognitive functioning (MMSE) was comparable in both studies, our aMCI group included 15 single-domain and 24 multiple-domain participants, which may explain why we observed impairment on both PM components. One might suppose that aMCI individuals in Delprado et al's study[30] mostly included single-domain aMCI individuals considering their PM deficits were more from difficulties on the RC. Despite these differences, our results are in line with previous findings that aMCI subjects exhibit greater PM deficits relative to naMCI and OA subjects[23,27] and that deficits in naMCI subjects were intermediate between OA and aMCI.[28] Research on PM is increasing in AD and MCI populations because functional and anatomical brain areas known to be impaired in these conditions parallel those involved in PM functioning. This study contributes to the existing literature in suggesting that executive functions as well as memory processes associated to PM are somewhat compromised in MCI and AD conditions, albeit at different levels.

A secondary objective of the present study was to examine if the envelope task would be an effective tool in discriminating between cognitively intact OA and those with compromised cognitive functioning. As expected, our study showed that the envelope task was highly sensitive and specific in detecting PM deficits among patients diagnosed with AD. Consistent with previous findings,[29] our results indicated that scores of 0 on the PC and ≤1 on the RC discriminated OA from AD patients with the greatest accuracy. Contrary to our predictions, these same cutoff values did not prove to be sensitive enough (although highly specific) in accurately discriminating OA from individuals with aMCI or naMCI. Establishing different cutoff values to better determine aMCI and naMCI group membership wasn't beneficial as this compromised the task's specificity without strengthening its sensitivity. Expanding from what was previously mentioned concerning the envelope task to be more linked to memory than executive functions, our results seem to follow a logical order in

that the task's sensitivity proves greatest among amnestic patients (AD), followed by aMCI patients as opposed to naMCI. One previous study[30] has reported fairly good indices of sensitivity and specificity by combining PC and RC scores into a total PM score (4 points) on the envelope task. Although some may adopt the latter scoring method, we consider separately evaluating the prospective and retrospective components and then dichotomizing PM performance to be a more preferred and valid approach, at least for determining AD group membership. It is believed the proposed cutoff values, as opposed to other alternatives, are more representative of the PM construct and more salient in a clinical perspective. In accordance with PM conceptualization,[1,2] a successful PC performance in this study combined values of 1 or 2 because it considers a trace of either intention to still be present in mind, sufficiently enough to spontaneously initiate a response, whereas a total failure on this component (PC score = 0) indicates a notable difficulty with self-initiated strategies[3] as well as the automatic associative memory system.[51,52] Stricter guidelines than those initially suggested in Huppert et al[29] were adopted for classifying unsuccessful performance on the RC because the inability to retrieve one intention or more, even with a cue, clearly indicates that episodic memory processes are impaired.

Limitations to our study include the variability in demographic characteristics within our sample as well as the small sample sizes in each of our groups. Increasing the number of participants would possibly allow analyses to be performed without dichotomizing the scores on the task and ultimately offer a clearer understanding on the cognitive impairment relative to each subgroup. In addition, this study included participants diagnosed with different etiologies (e.g. PD, iRBD) yielding to heterogeneous cognitive profiles within the MCI sample, and as a result rendering interpretation of results more challenging and complex. Also, patients included in this study were evaluated during an ON-medication phase and this might have played a role in altering their cognitive performance.

Overall, the present study has documented that the envelope task is a useful clinical tool for distinguishing between healthy older participants from those with an objective pathological cognitive profile. In a clinical perspective, although the envelope task's sensitivity seems to be weak within an aMCI population and even weaker within a naMCI population, it is a promising tool on the basis of its high specificity. A more sensitive measure may be needed to discriminate MCI from a normal cognitive profile, especially in the presence of mixed MCI subtypes. However, because clinicians are usually unaware of an individual's MCI subtype diagnosis until further investigation, the envelope task could still contribute to characterizing the neuropsychological profile. Compared with any other available PM measures (e.g. Cambridge Prospective Memory Test),[53] the envelope task can be administered in less than a minute and be easily embedded in a battery of neuropsychological tests. To date, it is the simplest of PM measures proven to quickly and effectively detect certain cognitive deficits that have serious implications in daily living (e.g. AD). Regarding a probable AD population, the envelope task is therefore definitely worth adopting in a clinical setting because it shows great discriminatory abilities. To our knowledge, this is the only study that has reported PM deficits across amnestic and nonamnestic MCI subtypes as well as AD patients using the envelope task. Among the many experimental and ecological PM instruments, the envelope task is practical, inexpensive (free of cost), quick to administer, and highly specific, which altogether merits further investigation in clinical and research settings alike.

DISCLOSURES

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