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The Relation Between Depressive Symptoms and Semantic Memory in Amnestic Mild Cognitive Impairment and in Late-Life Depression

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Abstract

Semantic deficits have been documented in the prodromal phase of Alzheimer's disease, but it is unclear whether these deficits are associated with non-cognitive manifestations. For instance, recent evidence indicates that cognitive deficits in elders with amnestic mild cognitive impairment (aMCI) are modulated by concomitant depressive symptoms. The purposes of this study were to (i) investigate if semantic memory impairment in aMCI is modulated according to the presence (aMCI-D group) or absence (aMCI group) of depressive symptoms, and (ii) compare semantic memory performance of aMCI and aMCI-D groups to that of patients with late-life depression (LLD). Seventeen aMCI, 16 aMCI-D, 15 LLD, and 26 healthy control participants were administered a semantic questionnaire assessing famous person knowledge. Results showed that performance of aMCI-D patients was impaired compared to the control and LLD groups. However, in the aMCI group performance was comparable to that of all other groups. Overall, these findings suggest that semantic deficits in aMCI are somewhat associated with the presence of concomitant depressive symptoms. However, depression alone cannot account solely for the semantic deficits since LLD patients showed no semantic memory impairment in this study. Future studies should aim at clarifying the association between depression and semantic deficits in older adults meeting aMCI criteria. (*JINS*, 2011, *17*, 865–874)

Keywords: Semantic memory, Famous person knowledge, Depression, Mild cognitive impairment, Late-life depression, Alzheimer's disease

INTRODUCTION

Episodic memory is typically the most impaired cognitive domain in elderly individuals with amnestic mild cognitive impairment (aMCI) (Petersen et al., 1999). However, several studies in recent years have shown that semantic deficits may also represent another aspect of memory that is affected in aMCI. For instance, deficits on semantic category fluency tasks occurred as early as 12 years before a diagnosis of AD was established in a population-based cohort of elderly individuals who were followed longitudinally (Amieva et al., 2008). Several studies have also shown that aMCI patients suffered from early breakdown of semantic knowledge of famous people, and that older patients who later on developed AD were initially more impaired at naming famous faces when compared to older adults who did not develop AD (Estevez-Gonzalez et al., 2004; Thompson, Graham, Patterson, Sahakian, & Hodges, 2002; Vogel, Gade, Stokholm, & Waldemar, 2005). In a recent study, aMCI and early AD patients were found to be similarly affected in terms of their

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ability to name faces and to provide semantic knowledge about famous people, when compared to healthy subjects. In addition, item analyses showed that the proper name anomia in aMCI patients was associated with underlying loss of semantic knowledge (Joubert et al., 2010).

Past studies have also demonstrated that clinical and cognitive factors can interact in the symptomatology of aMCI, and that these interdependent factors can play a role in the variability of the clinical presentation of aMCI. For instance, depression, which can be observed in nearly half of individuals with aMCI (Apostolova & Cummings, 2008), has been shown to be associated with the cognitive functioning of these individuals (Dierckx, Engelborghs, De Raedt, De Deyn, & Ponjaert-Kristoffersen, 2007; Bruce et al., 2008; Hudon, Belleville, & Gauthier, 2008). Hudon et al. (2008) showed that older adults with aMCI plus depressive symptoms (aMCI-D individuals) were more impaired on tests of executive functions than aMCI individuals with few or no depressive manifestations. In addition, based on secondary analyses, Dierckx et al. (2007) indicated that aMCI patients could be divided into two subgroups regarding their cued recall performance in an episodic memory task. While it is not clear whether these subgroups were different regarding depressive symptoms, Dierckx and colleagues highlighted that one subgroup performed similar to AD patients and the other subgroup performed similar to depressed elderly patients and healthy controls. These findings are consistent with those of Bruce et al. (2008), who found that depressive symptoms are associated with better memory performance in aMCI. Therefore, the relation between depressive symptoms and cognitive impairment in aMCI is not unidirectional in the sense that depressive symptoms are not necessarily associated with greater cognitive deficits. No study has yet investigated the relationship between depressive symptoms and semantic memory performance in aMCI, which may help gain a better understanding of the nature of semantic impairment in the preclinical phase of AD.

Another clinical condition associated with the presence of depressive symptoms in elderly individuals is known as late-life depression (LLD). The LLD syndrome is considered primarily as a disorder of mood as patients are diagnosed on the basis of the DSM-IV criteria for major depression (American Psychiatric Association, 1994). Like the concept of aMCI, LLD is associated with a high risk of developing AD (Jorm, 2000; van Reekum et al., 2005; Ownby, Crocco, Acevedo, John, & Loewenstein, 2006). Moreover, LLD patients generally show concomitant depressive and cognitive symptoms, just like aMCI-D individuals. But actually there is uncertainty as to whether LLD should be conceived as a "severe" form of aMCI-D or, alternatively, as a distinct syndrome (Panza et al., 2010; Simard, Hudon, & van Reekum, 2009). Comparing the neuropsychological deficits of LLD patients to that of aMCI-D persons should help clarifying this issue.

As opposed to aMCI patients, there is little evidence in the literature suggesting the presence of semantic deficits in LLD patients. Several studies have indicated that naming abilities are reduced in adults with major depression (King, Caine, Conwell, & Cox, 1991; Boone et al., 1994; Palmer et al., 1996). Even though naming may be associated at least in part with underlying semantic deficits, a study by Georgieff, Dominey, Michel, Marie-Cardine, and Dalery (1998) showed that anomia in major depression did not originate from degraded semantic representations but was rather related to a lexical access deficit. In other words, naming difficulties in depressive patients are related to the alteration of effortful retrieval processes (Georgieff et al., 1998). In aMCI, there is evidence that impairment of effortful processes explains to some extent the semantic deficits of patients (Duong, Whitehead, Hanratty, & Chertkow, 2006). However, aMCI patients likely present central deficits as well (Joubert et al., 2010). Thus, using tasks that minimize effortful processes should help differentiating aMCI, aMCI-D and LLD patients regarding semantic memory performance. As indicated below, the semantic task used in the current study was designed so as to provide maximum contextual information for subjects to carry out semantic judgments without requiring effortful retrieval processes.

Moreover, even though semantic deficits related to person-based knowledge have been documented in aMCI in recent years (Thompson et al., 2002; Estevez-Gonzalez et al., 2004; Vogel et al., 2005; Joubert et al., 2008, 2010), the precise nature of this impairment still remains poorly characterized. There are several lines of evidence suggesting that person knowledge may show a particular functional organization when compared to other domains of knowledge and this could explain to some extent why person knowledge is particularly prone to impairment in aMCI (Ahmed, Arnold, Thompson, Graham, & Hodges, 2008; Joubert et al., 2008, 2010).

The purpose of this study is thus two-fold: (i) investigate if semantic memory impairment in aMCI is modulated according to the presence (aMCI-D group) or absence (aMCI group) of depressive symptoms; and (ii) compare semantic memory performance of aMCI and aMCI-D groups to that of patients with LLD. Based on current evidence in the literature (e.g., results from Bruce et al., 2008 revealing that depressive symptoms are associated with better memory performance), our hypotheses are that semantic memory performance will be impaired in both aMCI and aMCI-D participants, but performance will be poorer in the absence of concomitant depressive symptoms. In regards to LLD patients, they will not show a semantic impairment.

METHODS

Subjects

Seventy-four subjects participated in the present study: 15 LLD patients, 17 aMCI patients, 16 aMCI-D patients, and 26 normal healthy controls. All subjects gave their written informed consent before participation. The research protocol was approved by the Research Ethics committee of the *Institut universitaire de gériatrie de Montréal* and of the *Institut universitaire en santé mentale de Québec*. All subjects

were aged 55 years and older, and their mother tongue was French.

Both subgroups of older adults with aMCI were referred by a team of trained neurologists, geriatricians, and psychiatrists who collaborated in this study. Before being referred, the patients received a routine clinical examination to exclude other (or non-AD) etiological conditions. Patients were identified on the basis of Petersen's latest criteria for the "amnestic" subtype of MCI (Petersen, 2004). Criteria included a memory complaint (corroborated by an informant when possible), which was confirmed with formal neuropsychological measures of episodic memory. Objective memory impairment was defined using a cutoff score of 1.5 standard deviations (*SD*) below the mean of age- and education-matched normal elderly subjects on a standardized measure of episodic memory. Finally, patients did not present significant alteration of activities of daily living and they failed to meet the diagnostic criteria for dementia. To identify the aMCI and aMCI-D subgroups, participants were administered the French version of the Geriatric Depression Scale (GDS; Bourque, Blanchard, & Vézina, 1990) and the median-split method was applied using the total GDS score. Using this method, patients with a GDS score ≤ 8 were included in the aMCI group and patients with a GDS score > 8 were included in the aMCI-D group. Recent evidence shows that a cutoff of 8 on the GDS is an optimal cutoff for screening of depressive symptoms in MCI populations (Debruyne et al., 2009). It is also important to emphasize that in the current study, depression in aMCI-D patients was subclinical (i.e., it did not meet any DSM-IV mood disorder criteria).

The LLD patients were also identified and referred by clinicians. These participants were older individuals who received a diagnosis of major depression based on the DSM-IV criteria (American Psychiatric Association, 1994). These criteria require the presence of five or more symptoms that have been present during the same 2-week period and that include at least a depressed mood and/or a markedly diminished interest or pleasure in all, or almost all, activities. Other symptoms can include disruptions of sleep, appetite, or thinking, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or guilt, and recurrent thoughts of death. These symptoms are not due to the direct physiological effects of a substance or to a general medical condition, and they cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. All LLD patients received antidepressant medication to stabilize their depressive mood. To maximize feasibility of neuropsychological testing, assessment of LLD patients was performed only when mood symptoms were stabilized using antidepressants. Indeed, due to the presence of profound distress and significant lack of motivation, cognitive assessment of LLD patients is very difficult when these persons are in the acute phase of depression or when they are untreated. The fact that all LLD patients were treated does not represent a major problem for results interpretation in the current study because there is evidence that cognitive deficits in these persons persist after treatment up to 4 years post-recovery. Furthermore, the persistent deficits affect multiple cognitive domains (Köhler, Thomas, Barnett, & O'Brien. 2010).

The control group consisted of healthy older adults recruited from the community. They showed normal cognitive functioning, as evidenced by their performance on a general neuropsychological battery (see below), and had no mood disorder. They were matched to patient groups on the basis of their age and educational level.

Exclusion criteria for all four groups of subjects were a history of neurological disease (including cerebrovascular disease), past or current psychiatric illness other than major depression, traumatic brain injury, history of alcoholism, untreated medical or metabolic condition, general anesthesia in the last 12 months, electroconvulsive therapy in the past 12 months, former intracranial surgery, and uncorrected hearing and vision problems.

Demographic data of the four groups of patients are presented in Table 1. The groups were comparable in terms of age and education.

Neuropsychological Assessment

To characterize the cognitive functioning of the groups, all participants underwent a comprehensive general neuropsychological assessment, which included standard neuropsychological measures of episodic memory, semantic memory, language, executive functions, visuospatial, and visuoperceptual abilities. Episodic memory was assessed with the *Test de rappel libre/rappel indicé à 16 items* (RL/RI-16) (Van der Linden et al., 2004), a free/cued word recall test widely used as a measure of verbal learning in French-speaking populations; the procedure of the RL/RI-16 is similar to the Free and Cued Selective Reminding Test (FCSRT) (Grober, Buschke, Crystal, Bang, & Dresner, 1988). General semantic memory was assessed with the pictures version of the Pyramids and Palm Trees Test (PPTT) (Howard & Patterson, 1992). Visual memory was assessed using the immediate recall (3 min) condition of the Rey complex figure (Rey, 1970). Language was assessed using the 15-item version of the Boston Naming Test (BNT) (Calero, Arnedo, Navarro, Ruiz-Pedrosa, & Carnero, 2002), as well as with Letter (T-N-P) and Category (animals) fluency tests (Consortium des Universités de Montréal et McGill, 1996). Executive functions were assessed using the California Stroop test (Delis, Kaplan, & Kramer, 2001). Visuoconstructional abilities were evaluated using the copy of the Rey–Osterrieth complex figure (Rey, 1970). Finally, visual perception was assessed using the size match task of the Birmingham Object Recognition Battery (BORB) (Riddoch & Humphreys, 1993).

Semantic Memory Test for Famous Persons

This task was used to verify the hypotheses mentioned above. The task was computerized and was carried out on a PC computer using the E-Prime software (Psychology Software Tools, Pittsburgh, PA). The semantic task provided maximum contextual support in order for subjects to carry out semantic judgments. The task began with a practice session

Table 1. Characteristics of controls, LLD, aMCI and aMCI-D patients.

	Controls ($n = 26$)	LLD ($n = 15$)	aMCI ($n = 17$)	aMCI-D ($n = 16$)	F (dl)	p
Demographic data						
Gender	4m/22f	3m/12f	7m/10f	10m/6f		
Age (years)	72,7 (5,3)	72,3 (10,6)	72,3 (6,8)	73,4 (8,0)	0,08 (3,70)	ns
Education (years)	13,2 (4,2)	13,4 (4,2)	13,1 (5,9)	12.9 (3,9)	0,04 (3,70)	ns
General cognitive functioning						
Dementia Rating Scale (144)	139.8 (2.9)	137.1 (6.1)	130.4 (8.3)[c]	133.4 (4.7)[b]	11.21 (3,70)	$p < 0.001$
MoCA (30)	27.9 (1.9)	25.9 (3.4)	22.8 (2.8)[c]	23.9 (2.5)[c]	15.17 (3,69)	$p < 0.001$
Depressive symptoms						
Geriatric Depression Scale (30)	3.6 (3.6)	8.9 (5.9)[c]	4.4 (2.3)	14.2 (3.3)[c,e]	28.97 (3,70)	$p < 0.001$
Vascular risk factor						
Hachinski	1.1 (1.4)	2.5 (2.3)[a]	0.9 (1.0)	1.4 (1.6)	2.90 (3,62)	$p < 0.05$
Memory						
RL/RI 16						
Immediate free recall of a word list (16)	10.6 (2.1)	9.7 (2.0)	3.4 (2.5)[c]	5.5 (2.2)[c]	44.99 (3,68)	$p < 0.001$
Immediate total recall of a word list (16)	15.5 (0.8)	15.0 (1.4)	9.1 (4.3)[c]	12.2 (2.5)[b,d]	27,16 (3,68)	$p < 0.001$
Delayed free recall of a word list (16)	12.9 (2.1)	10.9 (3.0)	3.6 (3.7)[c]	7.2 (3.2)[c,d]	36.67 (3,65)	$p < 0.001$
Delayed total recall of a word list (16)	15.9 (0.3)	15.1 (1.6)	9.7 (5.0)[c]	13.5 (2.3)[d]	18.12 (3,65)	$p < 0.001$
Rey-Osterrieth Immediate recall (36)	16.1 (4.5)	16.8 (6.6)	9.3 (6.5)[b]	10.5 (5.6)[a]	7.55 (3,67)	$p < 0.001$
Executive function						
California Stroop Test						
Part 3 (interference) (sec)	61.7 (11.4)	70.2 (26.2)	87.1 (41.3)[a]	79.4 (27.5)	3.14 (3,65)	$p < 0.05$
Part 3 (interference) (err)	1.0 (1.6)	2.3 (3.4)	2.6 (4.3)	3.2 (3.3)	1.74 (3,65)	ns
Part 4 (switching) (sec)	73.5 (17.6)	78.9 (28.5)	101.2 (46.8)[a]	89.6 (20.7)	3.07 (3,64)	$p < 0.05$
Part 4 (interference) (err)	1.5 (1.5)	3.9 (5.9)	6.4 (8.8)[a]	6.1 (5.8)	3.05 (3,64)	$p < 0.05$
Language and semantic memory						
Naming (Boston naming) (15)	13.7 (1.7)	13.3 (1.5)	13.2 (1.0)	11.9 (2.6)[b]	3.65 (3,69)	$p < 0.05$
Pyramids and Palm Trees Test (52)	49.6 (2.1)	49.1 (2.9)	49.7 (1.7)	45.7 (13.1)	1.47 (3,69)	ns
Verbal fluency "TNP" in 1 min	38.0 (11.8)	31.3 (11.5)	27.1 (12.8)[a]	30.9 (12.6)	3.05 (3,69)	$p < 0.05$
Category fluency "animals" in 1 min	21.2 (6.5)	16.5 (6.1)	13.1 (4.7)[c]	14.5 (3.9)[b]	8.82 (3,69)	$p < 0.001$
Visuoconstructional abilities						
Rey-Osterrieth Figure—Copy (36)	32.6 (3.2)	31.3 (4.2)	32.3 (2.5)	30.2 (3.1)	1.87 (3,67)	ns
Visuoperceptual abilities						
BORB—Size match task (30)	27.1 (1.7)	27.1 (2.4)	26.9 (2.2)	26.3 (2.0)	0.65 (3,69)	ns

LLD: Late-life depression; **aMCI**: amnestic Mild Cognitive Impairment; **aMCI-D**: amnestic Mild Cognitive Impairment with depressive symptoms. Results represent mean (*SD*) scores.
[a] $p < 0.05$ between control group and patient groups.
[b] $p < 0.01$ between control group and patient groups.
[c] $p < 0.001$ between control group and patient groups.
[d] $p < 0.01$ between aMCI and aMCI-D patients.
[e] $p < 0.001$ between aMCI and aMCI-D patients.

to ensure that the subject understood perfectly the following instructions: "You are going to see a series of names of famous persons presented one by one. You will have to answer YES or NO to each question regarding each famous person. Are you ready?". Thirty names of famous people were presented successively; they emanated randomly from various category groups including actors, singers, politicians and athletes from the local or international scene. Each name was presented individually. The subject had to answer three semantic questions about each famous person. Each question appeared individually on the computer screen below the name of the given celebrity. The three questions related to the *occupation*, the *nationality*, and a *unique biographical fact* about the famous person. A list of the stimuli is presented in Appendix, as well as examples of questions. Questions were formulated in such a way that the subject had to provide YES or NO answers. Subjects were required to provide an answer, even if they were unsure or believed they did not know the answer. There were as many correct statements as incorrect statements in the questions. Moreover, nationalities and occupations were counterbalanced, and presentation of the names of famous people was randomized for each subject.

Statistical Analyses

Neuropsychological and clinical tests

One-way analyses of variance (ANOVA) were calculated using the neuropsychological and clinical tests for the four groups of subjects. A Levene test was used to assess homogeneity of

variances. When variances were homogeneous, significant main effects were analyzed using Tukey's honestly significant difference (HSD). If the homogeneity of variance assumption was broken, the Welch F was used to determine significance and significant main effects were analyzed using Mann-Whitney *U*-tests.

Semantic memory test for famous persons

A mixed-measures ANOVA was calculated to compare the performances of the groups on the three semantic questions. If a significant interaction (type of question × group) was found according to the Greenhouse-Geisser criteria, which allow to correct for potential inhomogeneity of variance, a decomposition of the interaction was carried out to determine specifically for which type of questions there were significant differences between groups. For each semantic question for which a significant difference was found, *post hoc* analyses using the Sidak method were carried out to determine significant difference between groups. Finally, Pearson *r* correlations were calculated to estimate the associations between performances in the experimental semantic task and the clinical neuropsychological measures.

RESULTS

Neuropsychological and Clinical Assessment

Results of the clinical measures of the four groups of subjects and significant main effects are presented and summarized in Table 1. Results indicate that both aMCI groups had significantly lower scores than controls on the DRS and the MoCA. Also, as expected, LLD and aMCI-D patients had significantly higher score on the GDS compared to the controls. Additional non-parametric Mann-Whitney analyses did not reveal significant differences between males and females in any of the four groups in terms of GDS score (control group: Mann Whitney $U = 30$; $p = .31$; LLD group: $U = 7$; $p = .11$; MCI group: $U = 21$; $p = .17$; MCI-D group: $U = 18$; $p = .19$). Finally, only the LLD patients had a significant higher score than the controls on the Hachinski measure of vascular risk factors.

Results of the neuropsychological assessment of the four groups of subjects and significant main effects are also presented and summarized in Table 1. Results indicate that LLD patients did not differ significantly from controls on any measures of neuropsychological functioning. Regarding the aMCI and aMCI-D patients, both groups performed significantly worse than controls on verbal and visual episodic memory tests. Both aMCI groups also showed impairment relative to control participants on the category fluency test. In addition, aMCI patients were significantly impaired compared to controls on the California Stroop test, while aMCI-D patients were significantly impaired compared to controls on the Boston Naming test. Finally, both aMCI groups were more impaired than the LLD group at recalling the Rey Figure.

Semantic Memory Test for Famous Persons

Results for the semantic questionnaire, expressed in percentage of correct responses, are presented in Figure 1. The results of the mixed-measures ANOVA revealed a significant main effect of factor Type of question ($F(2,140) = 126.61$; $p < .001$) but not for factor Group ($F(3,70) = 2.40$; $p = .08$). The main effect was qualified by a significant interaction ($F(6,140) = 3.52$; $p < .001$). The decomposition of the interaction indicated a significant difference between groups for the question on *unique biographical knowledge* ($F(3,70) = 4.21$; $p < .01$), but not for the question on *occupation knowledge* ($F(3,70) = 2.10$; $p = .108$), or *nationality knowledge* ($F(3,70) = 0.81$; $p = .495$). Additional *post hoc* analyses using the Sidak method for the *unique biographical knowledge* revealed that aMCI-D patients performed significantly worse than controls ($p < .05$) and LLD patients ($p < .05$) (see Figure 1). Even though performance of the aMCI group was lower for *unique biographical knowledge*, the aMCI and LLD groups did not differ significantly from the control group on any of the three questions. In sum, as illustrated in Figure 1, performance on a test of famous person knowledge (especially unique biographical knowledge) was impaired in the aMCI-D group only.

We also examined patterns of responses among each group in terms of false positive *versus* false negatives errors. We found that the aMCI-D group had a slightly higher percentage of false-positive errors (FPE = 13.2%) than false-negative errors (FNE = 10.2%). This was also the case in the LLD group (FPE = 8.2%; FNE = 6.8%). The percentage of FPE and FNE was similar, however, in the aMCI group (FPE = 8.5%, FNE = 8.1%) and in the control group (FPE = 7.2%; FNE = 6.8%). The differences between groups, however, were not statistically significant.

Correlations Between Semantic Performance and Neuropsychological Performance

To determine if the performance of patients in the famous person semantic test was associated with effortful retrieval processes or executive functioning, correlation analyses were performed in the aMCI-D group, who was significantly impaired at the semantic task. Namely, correlations between performance in the famous persons test and performance in (i) the free recall condition of the RL/RI 16 test (total number of words retrieved); and (ii) the Inhibition and Flexibility conditions of the Stroop test (time to complete the task) were calculated. Results reveal non-significant correlations between performance in the famous person semantic test and free recall ($r(14) = -0.18$; $p = .56$), or executive (Stroop Inhibition condition: $r(14) = -0.05$; $p = .89$; Stroop Flexibility condition: $r(14) = -0.04$; $p = .87$) performance.

DISCUSSION

The objectives of this study were to (i) investigate whether semantic memory impairment in aMCI is modulated by

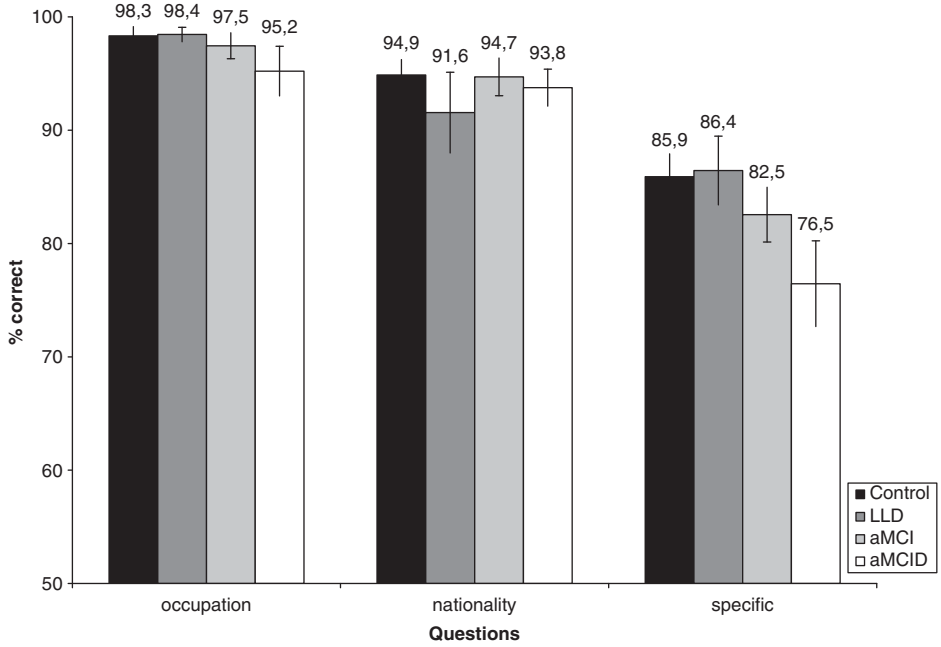

Fig. 1. Semantic performance accuracy for each group.

concomitant depressive symptoms and (ii) compare semantic memory performance of aMCI and aMCI-D groups to that of patients with LLD. Results showed that aMCI-D participants were impaired compared to LLD and control participants on the questions assessing *unique biographical knowledge*. As for the aMCI group, performance was not significantly different from that of all other groups. Overall, these findings suggest that semantic deficits in aMCI are associated to some extent with the presence of concomitant depressive symptoms. However, depression alone cannot account solely for the semantic deficits since LLD patients showed no semantic memory impairment in this study.

Semantic Memory and Depression

The nature of the episodic memory impairment in aMCI individuals has been widely investigated and represents one of the main diagnostic criteria according to international standards (Gauthier et al., 2006). More recently, semantic deficits have also been documented in aMCI individuals (e.g., Vogel et al., 2005; Joubert et al., 2008, 2010). Moreover, depressive symptoms have been shown to modulate the cognitive deficits in these individuals (Bruce et al., 2008; Hudon et al., 2008). To our knowledge, the present study is the first work documenting an association between depression and semantic memory in older adults meeting the aMCI criteria.

The present findings add to previous results which have documented person-based semantic deficits in aMCI patients (Joubert et al., 2008, 2010; Vogel et al., 2005). More precisely, this study reveals that impaired famous person knowledge in aMCI is linked to non-cognitive symptoms and, more particularly, to depression. This association between semantic impairment and depressive symptoms may be accounted for by the fact that older adults with aMCI-D show an increased risk of developing AD compared to aMCI patients without mood symptomatology (Modrego & Ferrandez, 2004). Second, it could be that aMCI and aMCI-D patients have distinct neuropathological characteristics (Panza et al., 2010) and these could explain to some extent the differences between groups at the cognitive level. Future studies should aim at replicating the present findings and, more importantly, at investigating whether aMCI and aMCI-D patients differ on a biological point of view.

Of interest, the present results showed that aMCI-D and LLD patients differed at the cognitive level. First, this suggests that depression alone cannot account solely for semantic memory impairment in older adults at risk of developing AD. Second, this may suggest that aMCI-D and LLD patients do not belong to the same nosological group. However, since the association between depression and cognitive impairment in older adults is a very complex issue (Steffens et al., 2006), it will be necessary to conduct longitudinal studies to verify this hypothesis. Moreover, it will be important to compare the patient groups on a series of biomarkers. Ultimately, such work should provide important insights to understand the associations between depression and cognitive impairment as well as the heterogeneity of the preclinical phase of AD.

This study corroborates previous findings which have shown that there is no degradation of semantic memory in LLD patients (Elderkin-Thompson, Boone, Hwang, & Kumar, 2004). As described in the Introduction and Methods sections, an effort was made in the present study to provide maximum contextual information in the semantic test to circumvent the deployment of effortful retrieval processes. Contrary to free recall tasks, which are known to be impaired in LLD (e.g., naming tasks, Georgieff et al., 1998), the

semantic test used in this study consisted of closed questions made of complete sentences that required only yes/no answers from participants, thereby minimizing the effortful processes required to retrieve information in semantic memory. The use of a semantic recognition test may thus logically explain the absence of semantic impairment in LLD found in the current study. Using the same framework, the semantic deficit observed in aMCI-D can hardly be explained in terms of effortful retrieval difficulties; the impairment rather seems to point to a more genuine semantic impairment reflecting mildly degraded semantic knowledge. This interpretation is supported by the results of the correlation analyses. In fact, we did not find any association between semantic deficits in the aMCI-D group and difficulties in effortful retrieval or executive functioning abilities. More studies are clearly needed to explore the complex relation that exists between semantic abilities and executive functions in patients with depressive symptoms. Finally, it is noteworthy to mention that there was no evidence of more random responding among aMCI-D patients compared to the other groups, that is, the proportions of false positive and false negative errors were comparable between the groups. Therefore, there were no significant differences between groups in terms of the strategies that were used to answer the semantic questions.

An interesting question is why the depressed aMCI group was more impaired than the other groups on the Boston Naming Test, yet did not differ from any of the groups on the Pyramid and Palms test, and how this relates to their performance on the famous person semantic test. Groups of participants in the present study were similarly affected on the BNT and on the famous person semantic test. In contrast, however, performance on the PPTT was similar across groups. This may be due to the fact that semantic deficits must be quite important before patients become impaired on this test (such as in semantic dementia for instance). Thus, the semantic deficits in aMCI patients may have been too mild to be detected with the PPTT. Moreover, there is recent evidence suggesting that the PPTT may lack reliability and validity (Klein & Buchanan, 2009). Alternatively, there may have been a mild lexical access problem in the depressed group, unrelated to any semantic deficit.

Famous Person Knowledge

In this study, aMCI-D patients were significantly impaired on questions tapping distinctive (unique biographical) knowledge, but not on questions tapping general (occupation, nationality) semantic knowledge. These findings can be interpreted from a theoretical point of view. That is, two types of models have been proposed to account for the organization of famous person knowledge. According to one view, biographical knowledge is organized in a categorical way (Burton, Bruce, & Johnstone, 1990; Stone, 2008) and is shared by different individuals. Alternatively, person knowledge may also be organized in an associative way (Schweinberger, 1996; Wiese & Schweinberger, 2011), depending on the patterns of association between a famous person and specific life events experienced by this person. In the current study, general semantic questions about the occupation and nationality were assumed to relate to a categorical organization, whereas unique semantic questions were assumed to be associative in nature. Results from the present study first support the notion that there are intrinsic differences (i.e., categorical *vs.* associative organization) in the cognitive architecture of person knowledge. Second, it suggests that unique/associative knowledge is more vulnerable in the context of cognitive decline. In other words, our results provide new insights on the organization of semantic memory and on the putative nature of the semantic breakdown in individuals at risk of developing AD.

Strengths and Limits

To our knowledge, this study is the first to investigate the relation between depressive symptoms and semantic deficits in aMCI. It is also the first to compare semantic processing in aMCI and aMCI-D *versus* LLD patients. Finally, contrary to several previous studies, the present word did not exclude aMCI participants with concomitant depression. These elements constitute important strengths. Indeed, our inclusion criteria helped depicting more extensively the variability of cognitive symptoms in older adults at risk of developing AD. Moreover, our study examined the similarities and differences in the associations among depression and mild cognitive impairment, as recommended by a group of experts convened by the National Institute of Mental Health (Steffens et al., 2006).

The principal limitation of the present study relates to the generalization of the results. For instance, exclusion criteria in participants' selection were extensive and this somewhat limits generalization of the results to the whole aMCI or LLD populations. In addition, the sample size was rather small and therefore we should consider the results of this study as preliminary evidence. This may account for instance for the absence of differences in semantic performance between the aMCI and aMCI-D groups. Larger groups will be necessary to determine if aMCI patients without depressive symptoms can be impaired in semantic tasks similar to that of the present work. It also appears that our semantic task may have lacked sensitivity to detect semantic deficits in non-depressed aMCI patients, such as indicated by some of the apparent ceiling effects that we observed for the semantic questions on occupation and nationality. Nonetheless, a significant impairment was found in the aMCI-D group for unique biographical questions, indicating that the semantic task in the present study was sensitive enough to detect subtle deficits. Another limitation of this study was the absence of direct assessment of anxiety symptoms, which are often associated with depression. It could be valuable to consider anxiety-related manifestations of depression in future studies to determine which types of non-cognitive symptoms are particularly linked to semantic deficits in aMCI-D patients. Moreover, studies of semantic priming which allow testing the semantic network implicitly would prove to be useful in determining whether semantic deficits in aMCI and aMCI-D

populations represent degraded semantic network or degraded elements of this network *versus* difficulties in accessing this network. Finally, one last point of caution in this study concerns the absence of documented semantic deficits in LLD patients. In fact, this latter group did not show significant cognitive deficits when compared to the healthy control group, nor did they show concomitant depressive symptoms at the time of testing. The possibility thus remains that the absence of semantic deficits in the LLD group may be due to the fact that they had completely recovered from their condition at this point in time.

In conclusion, this study shows that the presence of depressive symptoms modulates the presentation of semantic deficits in aMCI. Moreover, this presentation differs from that in LLD. Additional studies are still needed to better understand the complex relation between semantic impairment and depressive symptomatology in prodromal AD, and to help developing the theories behind the conceptual organization of person knowledge.

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APPENDIX

List of the famous persons that were used in the semantic memory test.

Name	Occupation	Nationality
René Lévesque	Politician	Canadian
Joseph-Armand Bombardier	Inventor	Canadian
Albert Einstein	Physicist	German
Robert Bourassa	Politician	Canadian
George W. Bush	Politician	American
Camillien Houde	Politician	Canadian
Michael Jackson	Singer	American
Céline Dion	Singer	Canadian
John F. Kennedy	Politician	American
Marilyn Monroe	Singer	American
Gilles Vigneault	Singer	Canadian
Jean Chrétien	Politician	Canadian
Elizabeth II	Politician	British
Maurice Richard	Athlete	Canadian
Pierre Elliott Trudeau	Politician	Canadian
Marlène Dietrich	Actress	German
Charlie Chaplin	Actor	British
Gilles Villeneuve	Athlete	Canadian
Franklin D. Roosevelt	Politician	American
Alfred Hitchcock	Producer	British
Louis de Funès	Singer	French
Maurice Duplessis	Politician	Canadian
Guy Lafleur	Athlete	Canadian
Humphrey Bogart	Actor	American
Jean Drapeau	Politician	Canadian
Jean Lesage	Politician	Canadian
Elvis Presley	Singer	American
Ginette Reno	Singer	Canadian
Charles Aznavour	Singer	Canadian
Wayne Gretzky	Athlete	Canadian

Examples of questions that were used in the semantic memory test

Joseph-Armand Bombardier

Est-ce que ce personnage a été un inventeur ? (*Was this person an inventor?*)

Est-ce que ce personnage est de nationalité anglaise? (*Is this person American?*)

Est-ce que cet personnage est considéré comme le père de l'Assurance-Maladie du Québec? (*Is this person considered to be the father of the Quebec Health Care System?*)

George W. Bush

Est-ce que ce personnage a été un politicien? (*Was this person a politician?*)

Est-ce que ce personnage est de nationalité canadienne? (*Is this person Canadian?*)

Est-ce que ce personnage a été le plus jeune Président élu aux États-Unis? (*Was this person the youngest president to be elected in the United-States?*)

Marilyn Monroe

Est-ce que ce personnage a été une politicienne? (*Was this person a politician?*)

Est-ce que ce personnage est de nationalité américaine? (*Is this person American?*)

Est-ce que ce personnage a épousé le joueur de baseball Joe DiMaggio? (*Was this person married to the baseball player Joe DiMaggio?*)