

Cognitive complaint in mild cognitive impairment and Alzheimer's disease

FRANCIS CLÉMENT,^{1,2} SYLVIE BELLEVILLE,^{1,2} AND SERGE GAUTHIER³

¹Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, Montréal, Canada

²Groupe de Recherche en Neuropsychologie et Cognition, Department of Psychology, Université de Montréal, Montréal, Canada

³McGill Centre for Studies in Aging, Montréal, Canada

(RECEIVED March 23, 2007; FINAL REVISION September 19, 2007; ACCEPTED September 20, 2007)

Abstract

Whereas the presence of a subjective memory complaint is a central criteria for mild cognitive impairment (MCI), little work has been done to empirically measure its nature and severity. The Self-Evaluation Questionnaire (QAM) assessed memory complaints relative to 10 domains of concrete activities of daily life in 68 persons with MCI, 26 persons with Alzheimer's disease (AD), and 81 healthy older adults. In addition, a neuropsychological battery was administered to assess whether subjective complaints were linked to actual cognitive performance. The findings indicate that individuals with MCI report more memory complaints than controls for a range of specific materials/circumstances. MCI and AD individuals did not differ in their level of memory complaints. Correlational analyses indicated that a higher level of memory complaints relative to conversations and to movies and books were associated with a higher level of objective cognitive deficits in persons with MCI but not in AD. Furthermore, complaints increased in parallel with global cognitive deficits in MCI. These results suggest that persons with MCI report more memory complaints than healthy older controls, but only in specific domains and circumstances, and that anosognosia is more characteristic of the demented than of the MCI phase of Alzheimer's disease. (*JINS*, 2008, *14*, 222–232.)

Keywords: Memory, Mild cognitive impairment, Neuropsychology, Dementia, Subjective complaint, Neuropsychological tests

INTRODUCTION

Mild cognitive impairment (MCI) has been identified as a risk factor for the development of AD as it has been shown that a large proportion of persons who meet the clinical criteria for MCI will progress to dementia (Gauthier et al., 2006). Typically, the criteria for MCI include the presence of an objective cognitive deficit relative to normative values and the presence of a subjective complaint (Petersen et al., 1999). In addition to being central to the defining criteria for MCI, the subjective complaint is also used by clinicians to support further investigation when there is suspicion of cognitive decline. Surprisingly, very little is known about the nature and severity of the cognitive complaints that characterize MCI.

One major objective of the present research was to assess the specific domains of complaint in persons with MCI. It

is now well established that individuals with MCI do not show general cognitive decline and that episodic memory is the cognitive domain for which they show the greatest impairments (Collie & Maruff, 2000; Nordahl et al., 2005; Perri et al., 2005; Petersen et al., 1999). Thus, it is expected that the reported cognitive problems of people with MCI relate to domains that require episodic memory. However, the majority of studies only examined a global level of memory complaints, and none have looked at specific domains of complaints. Such a global assessment approach could lead to misleading interpretations of the level of complaint. For instance, when asking one general question about subjective memory evaluation, Jungwirth et al. (2004) found that the majority (94%) of memory-impaired subjects did not complain about their memory, whereas Lam et al. (2005) obtained the opposite finding with a short (five questions) memory complaint questionnaire. This finding may result from the narrow set of questions or from the nature of the domains addressed by short questionnaires.

Correspondence and reprint requests to: Sylvie Belleville, Ph.D., Research Center, Institut Universitaire de Gériatrie de Montréal, 4565 Queen Mary, Montreal, H3W 1W5, Quebec, Canada. E-mail: sylvie.belleville@umontreal.ca

Another important objective in relation to complaints in MCI was to assess their actual predictive value of objective capacities. Previous findings are inconsistent regarding whether or not memory complaints are representative of the actual cognitive deficits in this population. Lam and collaborators (2005) found an association between memory complaint and cognitive test performances. Yet, other studies have found no association between self-reported memory complaint and objective memory deficits (Carr et al., 2000; Derouesne et al., 2004; Farias et al., 2005; Jungwirth et al., 2004). Again, the way in which memory complaints are measured is an issue. It is possible that relying on a comprehensive or focused assessment of the complaint affords a better fit with cognitive performance.

Finally, an important question to address relates to the changes that occur in the level and nature of complaint as individuals progress through the MCI phase, and from MCI to AD. First, it is well accepted that AD is characterized by anosognosia and that the level of anosognosia in AD increases with the severity of the disease (Kashiwa et al., 2005; Starkstein et al., 2006). This inverse relationship between complaint and cognition as the disease progresses is illustrated in Figure 1A. However, it is unclear how the cognitive com-

plaint evolves from MCI to AD and within the MCI phase. Whereas some studies have concluded that individuals with MCI and individuals with AD have a similar level of anosognosia (Vogel et al., 2004, 2005), others have found that persons with MCI report more cognitive problems (Kalbe et al., 2005) or functional difficulties (Farias et al., 2005) than what is reported by their informant, indicating an overestimation of their deficits. One possibility is that these differences are a function of the phase during which MCI participants were tested: the initial phase could be associated with a higher level of complaint, which would decrease as persons develop more severe deficits and anosognosia. This association would mimic the one found in AD and shown in Figure 1A. On the other hand, the complaint could increase along with the deficits during the MCI phase, as illustrated in Figure 1B, with anosognosia only appearing during the AD phase along with the emergence of executive impairment. Discrepancies could also relate to the domains for which persons with MCI are questioned. However, to our knowledge, no study has investigated the level and nature of the complaint within the MCI stage and as a function of the severity level of cognitive deficit.

In summary, the literature on the nature and level of complaint in MCI is sparse and the data are inconclusive. Several factors could explain the divergent findings found in the literature. Many studies investigated memory complaint with a limited set of questions (the number of questions often varying between one and five) or used a large-scale tool to measure cognition [e.g., Mini-Mental State Examination (MMSE)]. These are relevant factors because persons with MCI have mild cognitive decline, which may be obscured by the use of gross cognitive tasks. The modest cognitive impairment of MCI may result in more focused areas of difficulty, and thus, of complaints. For these reasons, more specific measures of the memory complaints that are specific to the MCI population are warranted. In addition, the complaint may change as MCI evolves toward AD, and severity has to be taken into account.

The goal of the present study was to investigate self-reported complaints related to cognition in everyday situations in normal elderly persons, persons with MCI, and persons with AD by taking into account the aforementioned factors. More importantly, we wanted to characterize the nature and severity of the cognitive complaint of MCI and AD persons and to determine whether this complaint is linked with their actual memory deficits and with the severity of their overall cognitive decline. We used the Self-Evaluation Questionnaire (QAM; Van der Linden et al., 1989) to assess self-reported complaints. The advantage of this questionnaire is that it contains a large number of questions grouped in sections that reflect different cognitive deficits: episodic memory, working memory, prospective memory, general events, face processing, orientation in space, and praxia. In addition, results from neuropsychological tests were used to assess how subjective complaint is associated with actual cognitive performance. We focused on episodic memory and executive functions as these are components that are impaired during the MCI phase (Belleville & Ménard, 2006; Hodges, 2006). The influence of depression

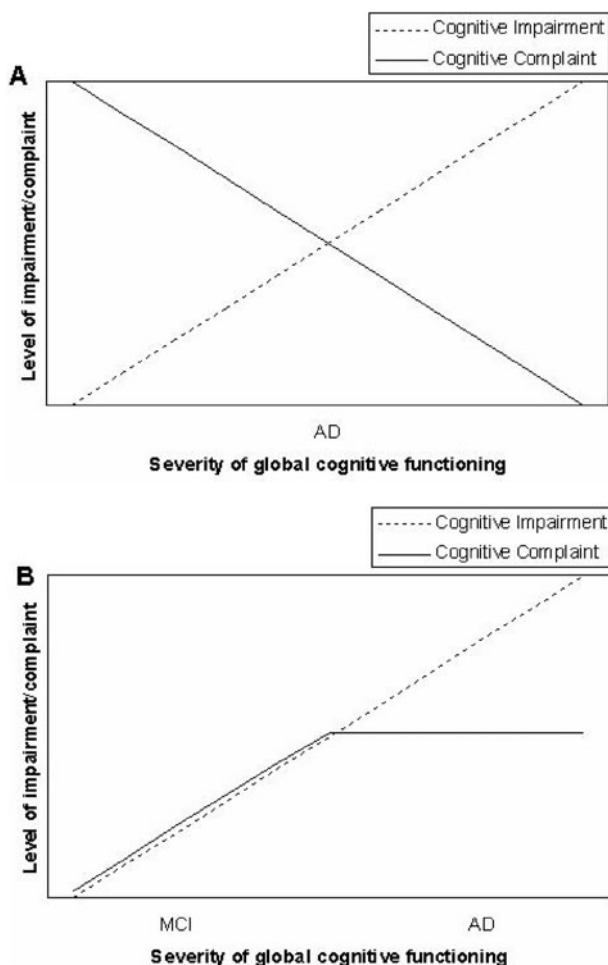


Fig. 1. Two possible models of the relationship between cognitive impairment and complaint in Alzheimer's disease.

on complaint was also measured. Psychoaffective symptoms could lead to an overestimation of the cognitive difficulties in persons with MCI in light of recent studies showing higher levels of anxiety and depression in these individuals (Gabryelewicz et al., 2004; Hwang et al., 2004; Kumar et al., 2006; Lopez et al., 2005; Lyketsos et al., 2002). Finally, the impact of progression in the disease and the role of the severity of cognitive deficits in complaint were measured. This was achieved by comparing the complaint in persons with MCI with that expressed by persons with AD, and by comparing the complaint in MCI persons with high and low global cognitive functioning.

We hypothesized that people with MCI would report more memory complaints than healthy older adults on the sections of the QAM that are indices of episodic memory and that their level of complaint would be equivalent or even more important than that of AD patients because individuals with AD are known to exhibit a certain degree of anosognosia. We also hypothesized that there would be an association between complaint and formal deficit in MCI and that persons with MCI who exhibit more severe cognitive impairments would show more cognitive complaints. However, no association was expected between complaint level and formal cognitive deficits in AD. Overall, this would be consistent with anosognosia appearing during the AD phase.

METHOD

Participants

A total of 175 participants, 26 AD patients, 68 persons with MCI, and 81 healthy older adults, participated in this study. Three persons with MCI and one healthy control did not

complete the entire QAM questionnaire and were thus excluded from some of the analyses. Healthy older adults (22 men) were between 50 and 87 years of age ($M = 68.6$; $SD = 8.2$), and had a mean of 14.2 years of education ($SD = 3.6$). Persons with MCI (29 men) were between 52 and 84 years of age ($M = 69.1$; $SD = 7.9$), with an average of 13.9 years of education ($SD = 4.3$), and persons with AD (13 men) were 51 to 85 years of age ($M = 74.5$; $SD = 7.7$) and had an average of 12.1 years of education ($SD = 5.0$). French was the first language of all participants.

Participants with AD and MCI were recruited from memory clinics where they had received their diagnosis following assessment by an experienced clinical neurologist and following extensive neuropsychological testing (see Table 1). In addition, AD and MCI participants went through an extensive medical, neurological, and neuroradiological examination to exclude the presence of any other significant systemic, neurological, or psychiatric condition that could explain their cognitive difficulties.

Participants with MCI met the criteria proposed by Petersen et al. (1999) for amnesic and nonamnesic types, single or multiple domains: (1) they consulted because they worried about their memory; (2) they performed at least 1.5 SD below the average level of persons of similar age and education on standardized memory tests (single domain amnesic MCI), on standardized memory and nonmemory tests (multiple domain amnesic MCI), or on standardized nonmemory tests (nonamnesic MCI); (3) they showed no global cognitive impairment on the basis of the MMSE; (4) nor any significant impact on daily functions as measured by the Functional Autonomy Measurement System (SMAF) functional impairment scale and clinical interview. Sixteen participants with MCI met the criteria for single domain

Table 1. Sociodemographic status and neuropsychological evaluation for the three groups

	Controls $n = 81$	MCI $n = 68$	AD $n = 26$
Age	68.59 (8.20)	69.06 (7.89)	74.50 (7.75)**
Education	14.19 (3.56)	13.88 (4.34)	12.12 (4.97)
MDRS	140.64 (2.89)	136.12 (4.95)**	120.88 (10.42)**
MMSE	28.91 (0.92)	27.96 (1.76)**	23.77 (3.64)**
GDS (/5)	0.70 (0.89)	1.09 (1.18)	1.23 (1.34)
Coding	11.00 (2.67)	9.22 (2.61)**	7.00 (3.01)**
Benton Judgment of line orientation	23.94 (3.87)	22.69 (4.69)	19.62 (5.89)**
BEM Immediate recall	8.93 (1.72)	6.51 (2.24)**	2.75 (1.72)**
BEM Delayed recall	8.64 (1.79)	5.82 (2.40)**	1.46 (1.78)**
SMAF	-0.17 (0.44)	-0.76 (0.77)	-4.74 (6.36)**
Copy of Rey's Figure: time	217.09 (96.26)	268.72 (122.09)	367.08 (204.79)**
Copy of Rey's Figure: score	32.09 (3.90)	29.43 (5.37)**	24.54 (7.14)**
Stroop 3rd plate time	29.27 (8.44)	35.11 (12.22)*	51.29 (20.86)**
Stroop 3rd plate errors	1.16 (1.43)	2.79 (3.02)**	4.85 (4.70)**
RL/RI-16 3rd free recall	11.88 (2.05)	8.94 (3.35)**	2.88 (2.72)**
RL/RI-16 delayed free recall	12.56 (2.31)	9.83 (3.55)**	2.38 (3.09)**

Note. SD is given in parentheses. Impairment relative to the controls at * $p < 0.05$, ** $p < 0.01$. MCI = mild cognitive impairment; AD = Alzheimer's disease; MDRS = Mattis Dementia Rating Scale; MMSE = Mini-Mental State Examination; GDS = Geriatric Depression Scale; BEM = *Batterie d'efficience mnésique*; SMAF = Functional Autonomy Measurement System; RL/RI-16 = a cued and free word recall task.

amnesic MCI, 49 met the criteria for multiple domain amnesic MCI, and 3 met the criteria for nonamnesic MCI. AD patients were diagnosed according to the NINCDS-ADRDA (McKhann et al., 1984) and Diagnostic and Statistical Manual for Mental Disorders-IV criteria. The severity of their disease ranged from mild to moderate, on the basis of the neuropsychological and clinical assessments. Elderly controls were recruited from the community. Healthy older adults also completed the clinical and neuropsychological assessment to ensure that they did not suffer from cognitive deficits. The study was approved by the Institut Universitaire de Gériatrie de Montréal Human Ethics Committee.

Memory Questionnaire

The Self-Evaluation Complaint Questionnaire (QAM; Van der Linden et al., 1989) is composed of 64 questions divided into 10 sections representing different dimensions of concrete activities and situations of daily life. The 10 sections are: 1, Conversation; 2, Movies and Books; 3, Slips of Attention; 4, People; 5, Use of Objects; 6, Political and Social Events; 7, Places; 8, Actions to Perform; 9, Personal Events; and 10, General. The sections cover a range of cognitive domains including episodic memory (1, Conversation; 2, Movies and Books), working memory (3, Slips of Attention), persons' knowledge (4, People), praxia (5, Use of Objects), knowledge about general events (6, Political and

Social Events), orientation in space (7, Places), prospective memory (8, Actions to Perform), autobiographical memory (9, Personal Events), and the impact of environmental/personal factors on memory (10, General). Each section includes 2 to 14 questions. For each question, participants make a judgment on a 6-point scale (from never = 1 to always = 6) about the frequency with which they encounter difficulties in a particular situation. A single score per section is determined by averaging the responses on all questions within the section. A total score, corresponding to the average score across sections, is also computed to assess the overall level of complaint. Examples of questions for each section are shown in Table 2.

Global Cognitive Function

The Mini-Mental State Examination (MMSE; Folstein et al., 1975) and the Mattis Dementia Rating Scale (MDRS; Mattis, 1976) were used to assess global functioning and dementia severity.

Functional and Psychological Assessment

The Functional Autonomy Measurement System (SMAF; Desrosiers et al., 1995) was used to measure functional autonomy. It is a 29-item scale that measures functional ability in five areas: activities of daily living, mobility, com-

Table 2. Examples of questions from each section of the QAM

Domains	Examples of questions
1. Conversation	Do you forget the content of a conversation that took place a few days before? Do you have difficulty following up on a conversation going on among many people because you forget what has just been said?
2. Movies and Books	Do you have difficulty in remembering the story of a movie seen a few days before? Do you have difficulty in reading because you forget what you have just read, which obliges you to read the same text again?
3. Slips of Attention	Do you forget to pick up personal objects when leaving a place? (e.g., keys, hat, etc.). Do you sometimes enter a room to do something and forget what it was that you wanted to do?
4. People	Do you have difficulty in remembering the name of a person you have met recently and still meet from time to time? Do you have difficulty in recognizing famous people's faces?
5. Use of Objects	Do you have difficulty in remembering how to appropriately use an object? Do you have difficulty in learning how to use an object you have never used before?
6. Political and Social Events	Do you have difficulty in remembering current events? Do you have difficulty in learning new knowledge (academic, professional, or other)?
7. Places	Do you have difficulty in learning a new itinerary? Do you forget the name of a street that you know well?
8. Actions to Perform	Do you forget to perform an action you planned on doing? Do you forget meetings?
9. Personal Events	Do you forget past personal events from a few days or weeks before? Do you hesitate to buy something because you are not sure if you already own it?
10. General	Is it more difficult for you to learn something while in a noisy environment? Is it more difficult for you to learn something when you are tired?

Note. QAM = Self-Evaluation Questionnaire.

munication, mental functions, and instrumental activities of daily living. A total disability score (on -87) was calculated for each subject. Depression was assessed using the short version (five items) of the Geriatric Depression Scale (GDS; Yesavage, 1988).

Memory

Memory was evaluated with a cued and free word recall task (RL/RI-16; Buschke, 1984; Van der Linden et al., 2004) and with a text memory of the BEM (Signoret, 1991). The RL/RI-16 allows for an assessment of patients' memory capacities when effective processing is provided during the learning of 16 words. There are three trials, with free recall followed by cued recall. A delayed free and cued recall is done after a 20-min delay. Text memory involves presentation of a short story followed by its immediate and delayed recall.

Executive Functions

Executive functions were evaluated with the third plate of Stroop-Victoria where participants are asked to name color words printed in noncorresponding colors of ink (Regard, 1981) and with the copy of Rey's complex figure. The score on the copy of the Rey's complex figure measures copy planning and strategy.

Data Analysis

Groups differences on sociodemographic factors were assessed with one-way analyses of variance (ANOVA) for the continuous variables age and education. Difference in gender composition was assessed with χ^2 . In the case of significant Group differences, further analyses included the relevant variable as a covariate.

To assess Groups differences on the QAM, a one-way multiple analysis of variance (MANOVA) was done using Group (controls, MCI, AD) as a between-subject factor on the scores of the 10 sections of the QAM. MANOVA is used in designs that have multiple dependent measures likely to be intercorrelated as is the case here. It forms a new dependant variable that is a linear combination of the measured dependant variables. It is thus a conservative test that reduces the likelihood of type 1 error (Tabachnick & Fidell, 2007). In the case of a significant group difference on the MANOVA, analysis of the location of the difference was done by performing individual ANOVAs on the individual scores for each section.

A correlational approach was used to test the relationship between subjective complaint on the QAM sections, depression, and cognitive performances. First, to reduce the number of variables, control for type 1 error and increase signal-to-noise ratio, performance on the cognitive tests were grouped to create three composite scores: a memory composite score, a composite score for the executive domain, and a severity composite. The cognitive tests were placed on the same scale by calculating individual Z-scores

using the mean and *SD* of the control group as a reference. The memory composite score was obtained by averaging the Z-scores on the BEM delayed recall, RL/RI-16 free recall Trial 3, and RL/RI-16 delayed free recall. The executive composite score was obtained by averaging Z-scores on Rey's complex figure (score) and Stroop-Victoria (number of errors: note that, to keep higher Z-scores as indicating higher performance, Z-scores for number of errors were reversed). The severity composite score was obtained by averaging the Z-scores on the MMSE and MDRS. It should be noted that a low severity score indicates low MMSE and MDRS scores and, thus, higher deficits of global cognitive function. Pearson's partial correlations were then computed between the QAM sections, the GDS, and three composite scores. We used only those sections for which significant MCI/Control group differences were found to reduce the number of comparisons. To control for type 1 error, a conservative *p* value of .005 was used as significance threshold.

The effect of overall cognitive deficit was assessed by separating participants with MCI into two groups: one with a higher level of overall cognitive functioning and one with a lower level of overall cognitive functioning. This was done using a split-median on the MDRS scores. The cognitive complaints of those with the highest MDRS scores ($n = 32$) were compared with the cognitive complaints of those with the lowest scores ($n = 33$) using a one-way MANOVA with Group (high-MDRS and low-MDRS) as a between-subject factor on the 10 sections of the QAM. The same procedure was used with AD patients.

RESULTS

Sociodemographic Data

To assess whether the groups differed on age, a one-way ANOVA with Group (controls, MCI, AD) as a between-subject factor was performed. The analysis indicated a main Group effect [$F(2, 172) = 5.65$; $p < .01$]. Post hoc tests indicated that AD patients were significantly older than controls and MCI, $p < .01$ in both cases. However, patients with MCI did not differ from controls. The age difference between patients with AD and persons with MCI is not surprising because MCI is considered to be a preclinical phase of AD. To assess whether age differences could account for our findings and whether age should be statistically controlled, a correlation was performed between age and the total number of complaints for each group. Age was not found to be significantly correlated with the number of complaints for any of our groups: $r = -0.19$, $r = -0.04$, $r = -0.09$, for AD, MCI, and controls, respectively. Thus, this factor was not taken into consideration in our future analyses.

A one-way ANOVA with Group (controls, MCI, AD) as a between-subject factor was also performed on education and indicated no Group differences [$F(2, 172) = 2.56$, N.S.]. A χ^2 analysis revealed that groups differed in their gender composition ($\chi^2 = 6.2$; $p < .05$). Therefore, gender was used as a covariate in all further analyses.

Validity of the QAM

To address the external validity of the QAM, the association between the QAM and the SMAF was assessed in healthy older adults, in MCI persons, and in AD patients. The QAM is a well-validated scale that measures the level of reported difficulties with complex activities of daily life (Desrosiers et al., 1995). A Pearson's partial correlation (controlling for gender) between the QAM total score and the score on the SMAF indicated a significant negative correlation between the two tests in healthy older adults ($r = -0.30, p < .01$), in persons with MCI ($r = -0.24, p < .05$), and in AD patients ($r = -0.45, p < .05$). In other words, a higher level of cognitive complaints on the QAM was associated with a lower score on the SMAF and, thus, with a lower level of self-reported functional autonomy.

Groups Differences on the QAM

Figure 2 displays the scores obtained by healthy older adults, persons with MCI and AD patients on each section of the QAM and their average scores. Inspection of Figure 2 indicates that persons with MCI and with AD reported more cognitive complaints than healthy controls. It also indicates heterogeneity across domains, as MCI persons and AD did not differ from healthy older adults on all sections of the QAM. This finding was confirmed by a one-way multiple analysis of covariance (MANCOVA) with Group (controls, MCI, AD) as a between-subject factor and gender as a covariate performed on the scores of the 10 sections of the QAM.

The MANCOVA indicated a significant main Group effect [$\Lambda = 0.77, F(20, 316) = 2.18, p < .01$]. ANOVAs indicated significant main Group effects on the following sections: Conversations [$F(2, 167) = 12.25, p < .001$], Movies and Books [$F(2, 167) = 7.88, p = .001$], Slips of Attention [$F(2, 167) = 3.23, p < .05$], Political and Social Events [$F(2, 167) = 3.06, p < .05$], Places [$F(2, 167) = 8.96, p < .001$], Personal Events [$F(2, 167) = 4.74, p = .01$], and General [$F(2, 167) = 3.16, p < .05$]. Tukey's post hoc tests indicated that individuals with AD and MCI reported a higher level of complaint than controls on the Conversation section ($p < .01$ in both groups), on the Movies and Books section ($p < .05$ and $p < .01$ for AD and MCI, respectively), and on the Places section ($p < .01$ in both groups). In addition, persons with MCI had a higher level of complaint than controls on the Slips of Attention section ($p < .05$), Personal Events section ($p < .01$), and on General section ($p < .05$). No significant differences between persons with MCI and AD were found on any of the sections.

Correlational Analyses

Correlations between cognitive tests and the QAM sections tested the relationship between complaint and cognitive deficits. The results obtained on the composite scores by patients with MCI and AD are shown in Table 3 (by definition, the average Z-score of control participants is 0).

To assess the relation between cognitive performance and the different domains of complaints, Pearson's partial correlations (controlling for gender) were computed between

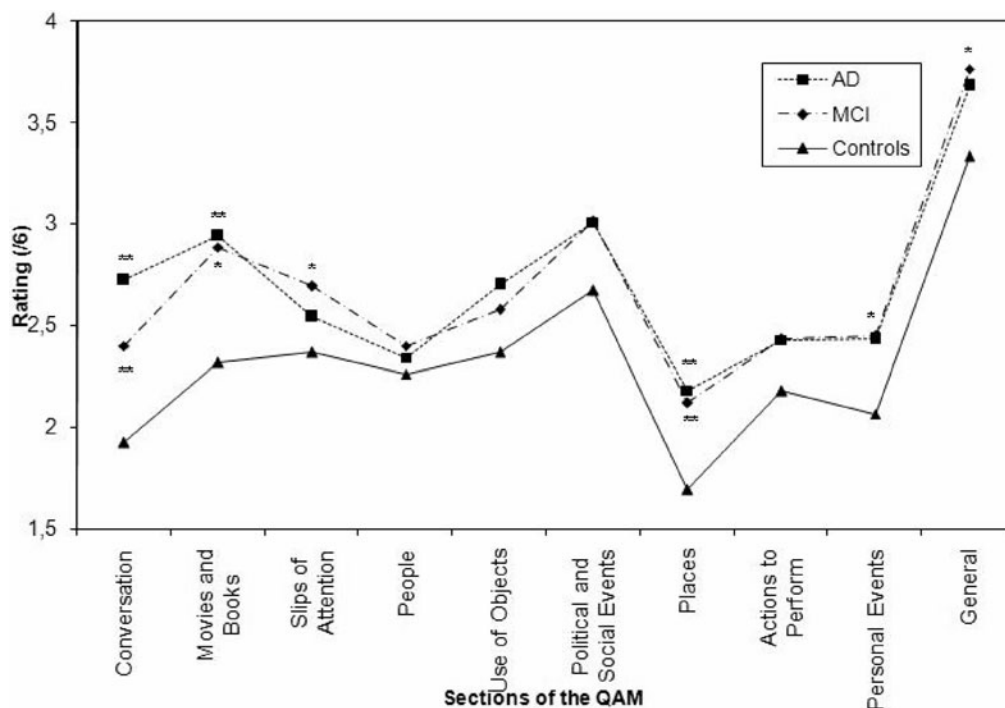


Fig. 2. Score obtained on the 10 sections of the Self-Evaluation Questionnaire (QAM) by persons with mild cognitive impairment (MCI), Alzheimer's disease (AD) patients, and control participants. * $p < .05$, ** $p < .01$.

Table 3. Mean Z-scores (and standard deviations) obtained by persons with MCI and AD

Scores	MCI <i>n</i> = 71	AD <i>n</i> = 26
Severity	−1.33 (1.53)**	−6.29 (3.39)**
Memory	−1.43 (1.29)**	−4.34 (1.11)**
Executive Functions	−0.93 (1.36)**	−2.30 (2.13)**

Note. Impairment relative to the controls at ** $p < .01$. MCI = mild cognitive impairment; AD = Alzheimer's disease.

the three composite scores and the QAM sections for which significant MCI/Control group differences were obtained (1, Conversation; 2, Movies and Books; 3, Slips of Attention; 7, Places; 9, Personal Events; 10, General). We also correlated the GDS with those sections of the QAM to assess the association between depression and cognitive complaint. The correlations are shown in Table 4. In persons with MCI, a higher level of complaints about Conversations (section 1) was associated with a lower global cognitive performance ($r = -0.39$, $p < .005$). In addition, the complaints relative to Movies and Books (QAM section 2)

were negatively correlated with the executive composite scores in persons with MCI ($r = -0.47$; $p < .005$; Table 4). Also, the complaints of AD patients relative to Slips of Attention (section 3) was positively correlated with the memory composite score ($r = 0.53$, $p < .005$). In healthy older adults, none of the domains of complaints correlated significantly with cognitive composite scores. Finally, in neither groups was depression associated with composite scores. [Because of the lack of a correlation between cognition and depression, it was unnecessary to perform an ANCOVA with this factor, despite the presence of a group difference on this factor (Lovell et al., 1987)].

MCI With High and Low Global Cognitive Functioning

We assessed whether or not individuals with MCI who had more severe global cognitive decline would report more memory complaints than those with better cognitive abilities. We used the MDRS scores as a measure of global cognitive functioning as it yielded the variability necessary for the use of a split-median and is not curtailed by ceiling effects. Furthermore, the MDRS investigates a broad range

Table 4. Correlations between QAM sections with GDS and scores of severity, memory, and executive functions

	GDS	Composite scores		
		Severity	Memory	Executive functions
Conversation				
MCI	0.14	−0.39*	−0.31	−0.29
AD	0.17	−0.21	0.16	−0.13
HC	0.08	−0.15	−0.18	0.12
Movies and Books				
MCI	0.05	−0.22	−0.27	−0.47*
AD	0.09	−0.26	0.14	−0.47
HC	0.06	−0.23	−0.26	0.09
Slips of Attention				
MCI	0.13	0.08	0.05	−0.22
AD	0.22	0.06	0.53*	−0.25
HC	0.22	−0.04	−0.09	0.08
Places				
MCI	0.16	−0.02	−0.10	−0.11
AD	0.12	−0.08	0.40	−0.23
HC	0.17	−0.09	−0.13	0.02
Personal Events				
MCI	0.08	−0.04	−0.09	−0.21
AD	0.18	−0.12	0.32	−0.24
HC	0.16	−0.09	−0.12	0.08
General				
MCI	0.13	−0.16	−0.24	−0.23
AD	0.08	−0.11	0.31	−0.29
HC	0.04	−0.23	−0.13	0.10

Note. QAM = Self-Evaluation Questionnaire; GDS = Geriatric Depression Scale; MCI = mild cognitive impairment; AD = Alzheimer's disease; HC = healthy control. * $p < .005$.

of cognitive functions and, hence, might be more sensitive to MCI's quite subtle cognitive impairments. A split-median on the MDRS distinguished participants with high and low global cognitive functioning. A one-way MANOVA with Group (high-MDRS and low-MDRS) as a between-subjects factor was then performed on the scores on the 10 sections of the QAM. A main group effect for the MANOVA was found [$\Lambda = 0.67$, $F(10,53) = 2.62$, $p < .05$]. A significant Group effect was found for the Conversations section [$F(1,62) = 5.99$, $p < .05$] and for Movies and Books [$F(1,62) = 4.31$, $p < .05$; Figure 3]. Therefore, persons with MCI who have lower global cognitive function on the MDRS report more memory problems related to conversations, and to movies and books, but not to other areas.

The same procedure was performed for the patients with AD patients. No main Group effect for the MANOVA was found.

DISCUSSION

The general goal of this study was to make a comprehensive assessment of self-reported complaints related to everyday cognitive situations in persons with MCI relative to normal elderly and AD patients, relate those to objective deficits and assess the effect of global cognitive deficits. Before discussing our main findings, we would like to stress that a moderate (negative) association was found between the QAM total score obtained by healthy older adults, MCI persons, and AD patients and their scores on a well-validated scale of functional autonomy. This finding confirms that a higher number of cognitive complaints was associated with poorer self-reported functional autonomy and, thus, provides some external validity for the QAM. Furthermore, none of our sections was correlated with the geriatric depression scale (GDS) in either groups, indicat-

ing that depression did not contribute to the data. These two preliminary findings are important as they indicate that the QAM reflects subjective self-assessment of cognitive impairment, but not a by-product of depressive symptoms.

A first objective of this study was to evaluate the level of complaints expressed by persons with MCI and AD on different domains of cognition. We found that complaints differed across domains. People with MCI report more memory problems related to Conversations (section 1), Movies and Books (section 2), Slips of Attention (section 3), Places (section 7), Personal Events (section 9), and on the General section (section 10). Most of these sections address problems that require encoding and retrieving the spatiotemporal context of information, a memory process particularly impaired in the MCI population (Collie & Maruff, 2000; Nordahl et al., 2005; Petersen et al., 1999). Thus, as predicted, subjective complaints are consistent with our knowledge regarding the nature of memory deficits in MCI. The level of complaint of AD patients was significantly higher than healthy controls in a subset of the domains for which MCI persons expressed complaints: Conversations, Movies and Books, and Places.

The second objective of this study was to evaluate the association between subjective and objective cognitive abilities measured by composite scores. It was found that only some domains of memory complaints in individuals with MCI were linked to their actual cognitive deficits: Conversations (section 1) was related to the global cognitive score and Movies and Books (section 2) was associated with the executive score. It indicates that a short complaint questionnaire that would include the questions that are part of those two sections (see Table 5 for the list of questions) may represent a good indicator of actual cognitive deficits. It is, however, important to note that none of the QAM sections were related to the memory composite score. Thus, persons

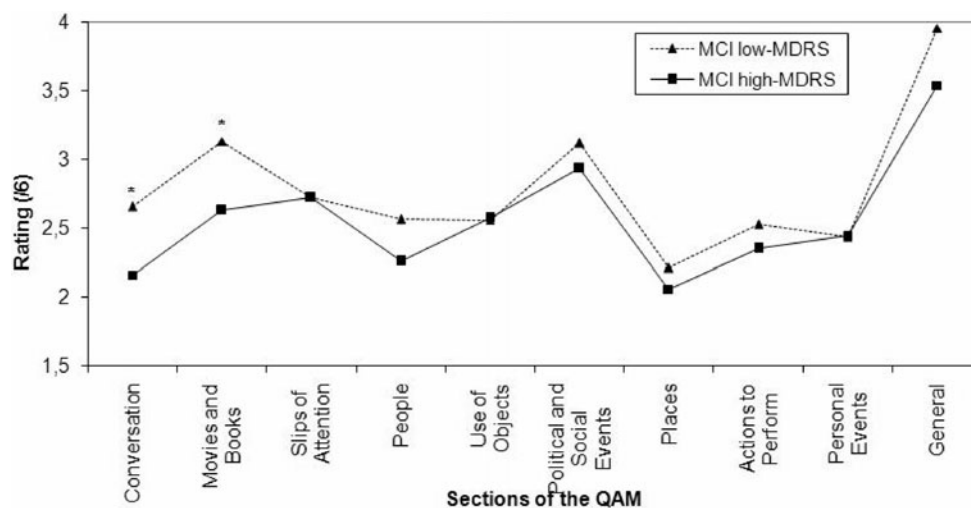


Fig. 3. Score obtained on the 10 sections of the Self-Evaluation Questionnaire (QAM) by individuals with mild cognitive impairment (MCI) with high Mattis Dementia Rating Scale (MDRS) scores and by individuals with MCI with low MDRS scores. * $p < .05$.

Table 5. Questions from sections Conversation and Movies and Books of the QAM

Domains	Questions
1. Conversation	Do you have difficulty in following up on a conversation going on with one person because you forget what has just been said? Do you have difficulty in following up on a conversation going on among many people because you forget what has just been said? During a conversation, do you repeat many times the same thing because you forgot that you have just said it? Does it happen that you repeat something again and again because you forget that you have already said it a few hours or a few days before? Do you forget the content of a conversation that took place a few days before? Do you forget the content of a conversation that has just taken place?
2. Movies and books	Do you have difficulty in reading because you forget what you have just read, which obliges you to read the text again? Do you have difficulty in remembering what you have read a few days before? Do you have difficulty in following a movie or a TV program because you forget what just happened? Do you have difficulty in remembering the story of a movie you have seen a few days before?

Note. QAM = Self-Evaluation Questionnaire.

with MCI complaint of memory deficits and these complaints are related to their general cognitive deficits but not to their actual memory deficits. This lack of a relationship between the QAM subscales and the memory composite score is in line with a recent study that shows that people with MCI have metamemory difficulties and are therefore poor at predicting their memory performance (episodic feeling-of-knowing; Perrotin et al., 2007). This finding may suggest that the complaint of persons with MCI is based on an assessment of their general cognitive difficulties and not on a precise assessment of their performance on memory.

We found no significant correlations between cognitive performance and the QAM subscales in healthy controls. This finding indicates that the relationship between cognition and memory complaint is specific to MCI. One possible reason for this lack of a correlation is that a large number of personal factors contributes to memory complaint in older adults without memory deficits. Possibly, it is only when a significant amount of memory change occurs—such as is the case in MCI—that this factor actually accounts for inter-individual variations in the level of complaint. There was also a remarkable absence of correlation between subjective complaints on memory domains and objective memory performance in AD patients. This finding is consistent with the anosognosia typically reported in AD patients (Farias et al., 2005; Kalbe et al., 2005). Notably, however, the number of AD participants in this study was relatively small ($n = 26$) and more statistical power might be required to uncover an association between objective deficits and cognitive complaints in AD. Hence, these results need to be replicated with a larger sample.

One final goal was to investigate the differences in the level and nature of cognitive complaint as a function of the severity of cognitive impairment in MCI and AD. We are aware that the level of severity measured in a cross-sectional sample cannot be entirely amenable to progression in the disease. However, our hypothesis was that participants with more severe overall cognitive deficit were

more likely to be more advanced along the MCI/AD continuum. On that basis, it was predicted that individuals with MCI who exhibited more severe cognitive impairments would show more cognitive complaints and that anosognosia would only be present in participants with AD. The results of this study partially confirm this hypothesis: MCI persons who had larger cognitive deficits report more problems with Conversation and with Movies and Books than those with smaller cognitive deficits. In addition, there is a correlation between the composite score of severity and the level of complaint on Section 1 (Conversation). This finding supports an increase in the complaint that parallels the cognitive decline during the MCI phase. Our data also suggest that the complaint does not increase further as patients progress into the AD phase. This relation between complaint and deficit during the MCI/AD continuum is illustrated in Figure 1B.

We are aware of the limitations of this study. First, as mentioned above, our sample of AD patients was relatively small and we may have lacked some statistical power for this population. That participants with AD and MCI were recruited from memory clinics can also be judged as a limitation. Specifically, our sample is biased toward persons who consulted the clinics themselves and are thus somehow more sensitive to their problems, at least on a general level. It would be interesting to extend our results to a community-based sample that would include people who did not consult for their memory problems. A related limitation arises from the apparent circularity of the studying of memory complaint in a diagnostic category that contains memory complaint as a criteria. However, circularity is reduced by the fact that our goal was to characterize the specific domains of complaint in MCI and to assess the relationship between cognitive complaint and actual deficits as well as its change as a function of overall disease severity, rather than just confirm the presence of a complaint. Again, extending our results to a community-based sample would protect against circularity. A third limitation

is the cross-sectional design of the study, which does not permit us to attribute direct causation between our variables, and which limits the interpretation of our findings in terms of progression. These individuals with MCI, as well as the patients with AD, are currently being followed-up, which might allow us to obtain more conclusive results in the future. Also, we did not give the QAM to informants. Notably, however, the format of the questionnaire is not easily amenable to a third-party, because some questions are specific to mental states and may not be evaluated from an outside point-of-view.

Overall, the findings of our study indicate that individuals with MCI report more memory complaints than healthy older controls, but only in specific domains and circumstances. Within these specific domains of complaint, only two (reported memory difficulties for conversations, and for movies and books) were found to be good indicators of their objective cognitive deficits, to increase in parallel with global cognitive deficits in MCI and to reach a plateau once the individual has progressed to AD. The complaints related to these two domains appear more relevant and better indicators of global cognitive deficits than other memory domains probably because they place a high demand on episodic memory processes.

ACKNOWLEDGMENTS

This work was supported by a National Research Award from the FRSQ to S.B. and by a grant from the CIHR to S.B. F.C. was supported by a scholarship from the Fond Québécois de la Recherche sur la Nature et les Technologies (FQRNT). We thank Sara Bélanger for her suggestions and comments, Émilie Lepage for the neuropsychological evaluation of the participants, and Janet Boseovski and Harold Gaboury for editorial assistance. The authors have reported no conflicts of interest.

REFERENCES

- Belleville, S. & Ménard, M.-C. (2006). Neuropsychologie du trouble cognitif léger ou mild cognitive impairment. In C. Belin, A.-M. Ergis, & O. Moreau (Eds.), *Actualités sur les démences: Aspects cliniques et neuropsychologiques* (pp. 613–629). Marseille: Solal.
- Buschke, H. (1984). Cued recall in amnesia. *Journal of Clinical Neuropsychology*, 6, 433–440.
- Carr, D.B., Gray, S., Baty, J., & Morris, J.C. (2000). The value of informant versus individual's complaints of memory impairment in early dementia. *Neurology*, 55, 1724–1726.
- Collie, A. & Maruff, P. (2000). The neuropsychology of preclinical Alzheimer's disease and mild cognitive impairment. *Neuroscience and Biobehavioral Reviews*, 24, 365–374.
- Derouesne, C., Rapin, J.R., & Lacomblez, L. (2004). Memory complaints in 200 subjects meeting the diagnostic criteria for age-associated memory impairment: Psychoaffective and cognitive correlates. *Psychologie Neuropsychiatrie du Vieillessement*, 2, 67–74.
- Desrosiers, J., Bravo, G., Hebert, R., & Dubuc, N. (1995). Reliability of the revised functional autonomy measurement system (SMAF) for epidemiological research. *Age and Ageing*, 24, 402–406.
- Farias, S.T., Mungas, D., & Jagust, W. (2005). Degree of discrepancy between self and other-reported everyday functioning by cognitive status: Dementia, mild cognitive impairment, and healthy elders. *International Journal of Geriatric Psychiatry*, 20, 827–834.
- Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189–198.
- Gabryelewicz, T., Styczynska, M., Pfeffer, A., Wasiak, B., Barczak, A., Luczywek, E., Androsiuk, W., & Barcikowska, M. (2004). Prevalence of major and minor depression in elderly persons with mild cognitive impairment—MADRS factor analysis. *International Journal of Geriatric Psychiatry*, 19, 1168–1172.
- Gauthier, S., Reisberg, B., Zaudig, M., Petersen, R.C., Ritchie, K., Broich, K., Belleville, S., Brodaty, H., Bennett, D., Chertkow, H., Cummings, J.L., de Leon, M., Feldman, H., Ganguli, M., Hampel, H., Scheltens, P., Tierney, M.C., Whitehouse, P., & Winblad, B. (2006). Mild cognitive impairment. *Lancet*, 367, 1262–1270.
- Hodges, J.R. (2006). Alzheimer's centennial legacy: Origins, landmarks and the current status of knowledge concerning cognitive aspects. *Brain*, 129(Pt 11), 2811–2822.
- Hwang, T.J., Masterman, D.L., Ortiz, F., Fairbanks, L.A., & Cummings, J.L. (2004). Mild cognitive impairment is associated with characteristic neuropsychiatric symptoms. *Alzheimer Disease and Associated Disorders*, 18, 17–21.
- Jungwirth, S., Fischer, P., Weissgram, S., Kirchmeyr, W., Bauer, P., & Tragl, K.H. (2004). Subjective memory complaints and objective memory impairment in the Vienna-Transdanube aging community. *Journal of the American Geriatric Society*, 52, 263–268.
- Kalbe, E., Salmon, E., Perani, D., Holthoff, V., Sorbi, S., Elsner, A., Weisenbach, S., Brand, M., Lenz, O., Kessler, J., Luedecke, S., Ortelli, P., & Herholz, K. (2005). Anosognosia in very mild Alzheimer's disease but not in mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders*, 19, 349–356.
- Kashiwa, Y., Kitabayashi, Y., Narumoto, J., Nakamura, K., Ueda, H., & Fukui, K. (2005). Anosognosia in Alzheimer's disease: Association with patient characteristics, psychiatric symptoms and cognitive deficits. *Psychiatry and Clinical Neurosciences*, 59, 697–704.
- Kumar, R., Parslow, R.A., Jorm, A.F., Rosenman, S.J., Maller, J., Meslin, C., Anstey, K.J., Christensen, H., & Sachdev, P.S. (2006). Clinical and neuroimaging correlates of mild cognitive impairment in a middle-aged community sample: The personality and total health through life 60+ study. *Dementia and Geriatric Cognitive Disorders*, 21, 44–50.
- Lam, L.C., Lui, V.W., Tam, C.W., & Chiu, H.F. (2005). Subjective memory complaints in Chinese subjects with mild cognitive impairment and early Alzheimer's disease. *International Journal of Geriatric Psychiatry*, 20, 876–882.
- Lopez, O.L., Becker, J.T., & Sweet, R.A. (2005). Non-cognitive symptoms in mild cognitive impairment subjects. *Neurocase*, 11, 65–71.
- Lovell, M., Franzen, M.D., & Golden, C.J. (1987). Statistical techniques in neuropsychology, IV: Analysis of covariance. *The International Journal of Clinical Neuropsychology*, 9, 49–55.
- Lyketsos, C.G., Lopez, O., Jones, B., Fitzpatrick, A.L., Breitner, J., & DeKosky, S. (2002). Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: Results from

- the cardiovascular health study. *Journal of the American Medical Association*, 288, 1475–1483.
- Mattis, S. (1976). Mental status examination for organic mental syndrome in the elderly patient. In L. Bellak & T.B. Karasu (Eds.), *Geriatric psychiatry*. New York: Grune & Stratton.
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E.M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services task force on Alzheimer's disease. *Neurology*, 34, 939–944.
- Nordahl, C.W., Ranganath, C., Yonelinas, A.P., DeCarli, C., Reed, B.R., & Jagust, W.J. (2005). Different mechanisms of episodic memory failure in mild cognitive impairment. *Neuropsychologia*, 43, 1688–1697.
- Perri, R., Carlesimo, G.A., Serra, L., & Caltagirone, C. (2005). Characterization of memory profile in subjects with amnesic mild cognitive impairment. *Journal of Clinical and Experimental Neuropsychology*, 27, 1033–1055.
- Perrotin, A., Belleville, S., & Isingrini, M. (2007). Metamemory monitoring in mild cognitive impairment: Evidence of a less accurate episodic feeling-of-knowing. *Neuropsychologia*, 45, 2811–2826.
- Petersen, R.C., Smith, G.E., Waring, S.C., Ivnik, R.J., Tangalos, E.G., & Kokmen, E. (1999). Mild cognitive impairment: Clinical characterization and outcome. *Archives of Neurology*, 56, 303–308.
- Regard, M. (1981). *Cognitive rigidity and flexibility: A neuropsychological study*. Victoria, BC, Canada: University of Victoria.
- Signoret, J.L. (1991). *Batterie d'efficience mnésique bem 144*. Paris: Elsevier.
- Starkstein, S.E., Jorge, R., Mizrahi, R., & Robinson, R.G. (2006). A diagnostic formulation for anosognosia in Alzheimer's disease. *Journal of Neurology Neurosurgery, and Psychiatry*, 77, 719–725.
- Tabachnick, B.G. & Fidell, L.S. (2007). *Using multivariate statistics*. Boston: Pearson Education.
- Van der Linden, M., Adam, S., Agniel, A., Baisset-Mouly, C., Bardet, F., Coyette, F., Desgranges, B., Deweer, B., Ergis, A.M., Gély-Nargeot, M.C., Grimompres, L., Juillerat, A.C., Kalafat, M., Poitrenaud, J., Sellal, F., & Thomas-Antérion, C. (2004). *L'évaluation de troubles de la mémoire: Présentation de quatre tests de mémoire épisodique (avec étalonnage)*. Marseille, France: Solal.
- Van der Linden, M., Wijns, C., Von Frenkell, R., Coyette, F., & Seron, X. (1989). *Un questionnaire d'auto-évaluation de la mémoire (qam)*. Bruxelles, Belgium: Editest.
- Vogel, A., Hasselbalch, S.G., Gade, A., Ziebell, M., & Waldemar, G. (2005). Cognitive and functional neuroimaging correlate for anosognosia in mild cognitive impairment and Alzheimer's disease. *International Journal of Geriatric Psychiatry*, 20, 238–246.
- Vogel, A., Stokholm, J., Gade, A., Andersen, B.B., Hejl, A.M., & Waldemar, G. (2004). Awareness of deficits in mild cognitive impairment and Alzheimer's disease: Do MCI patients have impaired insight? *Dementia and Geriatric Cognitive Disorders*, 17, 181–187.
- Yesavage, J.A. (1988). Geriatric depression scale. *Psychopharmacological Bulletin*, 24, 709–711.