Neuropsychologia 48 (2010) 978–988

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

The cognitive and neural expression of semantic memory impairment in mild cognitive impairment and early Alzheimer's disease

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ARTICLE INFO

Article history:
Received 2 February 2009
Received in revised form
10 November 2009
Accepted 24 November 2009
Available online 30 November 2009

Keywords:
Semantic memory
Naming
Mild cognitive impairment
Alzheimer's disease

ABSTRACT

Semantic deficits in Alzheimer's disease have been widely documented, but little is known about the integrity of semantic memory in the prodromal stage of the illness. The aims of the present study were to: (i) investigate naming abilities and semantic memory in amnestic mild cognitive impairment (aMCI), early Alzheimer's disease (AD) compared to healthy older subjects; (ii) investigate the association between naming and semantic knowledge in aMCI and AD; (iii) examine if the semantic impairment was present in different modalities; and (iv) study the relationship between semantic performance and grey matter volume using voxel-based morphometry. Results indicate that both naming and semantic knowledge of objects and famous people were impaired in aMCI and early AD groups, when compared to healthy age- and education-matched controls. Item-by-item analyses showed that anomia in aMCI and early AD was significantly associated with underlying semantic knowledge of famous people but not with semantic knowledge of objects. Moreover, semantic knowledge of the same concepts was impaired in both the visual and the verbal modalities. Finally, voxel-based morphometry analyses revealed that semantic impairment in aMCI and AD was associated with cortical atrophy in the anterior temporal lobe (ATL) region as well as in the inferior prefrontal cortex (IPC), some of the key regions of the semantic cognition network. These findings suggest that the semantic impairment in aMCI may result from a breakdown of semantic knowledge of famous people and objects, combined with difficulties in the selection, manipulation and retrieval of this knowledge.

1. Introduction

Semantic memory concerns general world knowledge, acquired over a lifetime and shared by a same cultural group. It includes for instance knowledge about objects, people, places, concepts, facts and language. Semantic deficits have been documented in Alzheimer's disease (AD) using a variety of standard clinical neuropsychological tests, such as confrontation naming (Huff, Corkin, & Growdon, 1986), visual–verbal semantic matching (Hodges & Patterson, 1995) and category fluency (Adlam, Bozeat, Arnold, Watson, & Hodges, 2006; Rosser & Hodges, 1994). Studies which have investigated semantic breakdown in AD using more sensitive experimental measures have also shown that subordinate knowledge is more impaired than superordinate knowledge (Chertkow & Bub, 1990; Hodges, Patterson, Oxbury, & Funnell, 1992), that biological entities are more affected than non-biological entities (Fung et al., 2001; Gonnerman, Andersen, Devlin, Kempler, & Seidenberg, 1997; Whatmough et al., 2003), and that knowledge of famous people is disproportionately impaired relative to other categories of conceptual knowledge and to autobiographical memory (Greene & Hodges, 1996; Thompson, Graham, Patterson, Sahakian, & Hodges, 2002).

Clinical research has shown that AD is often preceded by a clinical phase commonly referred to as amnestic mild cogni-

Abbreviations: aMCI, amnestic mild cognitive impairment; MMSE, Mini-Mental State Examination; AD, Alzheimer's disease; VBM, voxel-based morphometry.

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doi:10.1016/j.neuropsychologia.2009.11.019

tive impairment (aMCI) (Gauthier et al., 2006; Petersen, 2003). Although, as in AD, episodic memory impairment is considered to be the main clinical feature of aMCI, recent studies have demonstrated the presence of semantic memory impairment as well (Adlam, Bozeat, Arnold, Watson, & Hodges, 2006; Ahmed, Arnold, Thompson, Graham, & Hodges, 2008; Duong, Whitehead, Hanratty, & Chertkow, 2006; Estevez-Gonzalez et al., 2004; Joubert et al., 2008; Seidenberg et al., 2009; Vogel, Gade, Stokholm, & Waldemar, 2005). For instance, several studies have shown that aMCI patients suffered from early breakdown of semantic knowledge of famous people. Predementia patients who later on converted to AD were initially more impaired at naming famous faces relative to the non-converters (Estevez-Gonzalez et al., 2004; Thompson et al., 2002; Vogel et al., 2005). Recently, Ahmed et al. (2008) demonstrated that naming photographs of famous people and famous buildings was significantly more impaired than naming of line drawings of common objects in aMCI individuals. The authors suggested that semantic knowledge about unique entities such as famous people and buildings may be more vulnerable to damage than more general knowledge about common objects. We also found such evidence in aMCI patients and demonstrated that the fine-grained semantic processing of entities which have unique idiosyncratic attributes may be affected earlier and to a greater extent than the semantic processing of generic concepts (Joubert et al., 2008). Similarly, using experimental measures of object naming, a study showed in preclinical AD patients that impaired naming of famous faces was more predictive of future conversion to AD than object naming (Thompson et al., 2002).

Overall, these studies have demonstrated that naming pictures of unique entities including famous people, famous buildings and famous public events is significantly more affected in aMCI individuals than picture naming of common objects. Although anomia for famous people has been documented in recent years, little is still known about the integrity of semantic knowledge in aMCI. Most studies in aMCI patients have been descriptive, i.e., they have reported that aMCI patients were impaired on naming tasks, without assessing what mechanisms were associated with this impairment. The first objective of this study is to evaluate the naming deficits and the semantic deficits in aMCI patients compared to early AD and normal controls. The possibility that aMCI patients present with genuine semantic memory impairment remains unclear at this point in time, although there is now some indication that this may be so several years before conversion to dementia (Amieva et al., 2008). The second objective is to investigate if there is an association between anomia and impaired semantic knowledge in aMCI. The third objective is to examine if the same concepts are impaired in different modalities in aMCI, i.e., visual and verbal, which may provide evidence of a central breakdown of semantic knowledge. Finally, we also carried out an imaging study to verify if the semantic deficits observed in these patients correlated with atrophy in brain regions known to be important for semantic memory.

2. Methods

2.1. Subjects

Three groups of right-handed subjects participated in the present study: 15 aMCI patients, 16 early AD patients and 16 healthy elderly controls. All subjects gave their written informed consent before participation. The research protocol was approved by the Research Ethics committee of Institut universitaire de gériatrie de Montréal (IUGM). Considering the cultural sensitivity of semantic tests, all participants were required to have lived at least the last 40 previous years of their lives in Quebec and their mother tongue was French.

The aMCI group consisted of 15 elderly subjects (8 females and 7 males) referred to the Cognition clinic of the IUGM in Montreal. MCI patients were seen at the memory clinic by a team of trained neurologists, geriatricians, and clinical neuropsychologists and they were identified on the basis of Petersen's (2001) criteria. Criteria included normal activities of daily living as assessed during a clinical interview and defined by a score of 0 on the IADL (independent activities of daily living) (Lawton & Brody, 1969), and an MMSE (Mini-Mental State Examination) score ≥25 (Folstein, Folstein, & McHugh, 1975). Criteria included a memory complaint corroborated by an informant and confirmed with formal neuropsychological measures of episodic memory. An objective memory impairment was defined by impaired performance using a cut-off score of 1.5 standard deviations (S.D.) below the mean of matched normal elderly subjects on standard measures of episodic memory. Here, we used the test de rappel libre/rappel indicé à 16 items (RL/RI 16) (Van der Linden et al., 2004), a test of episodic memory in French similar to the free and cued selective reminding test (FCSRT) (Grober, Buschke, Crystal, Bang, & Dresner, 1988). Finally, MCI patients were not sufficiently impaired cognitively or functionally to meet criteria for AD or dementia. The AD group consisted of 16 subjects (9 females and 7 males) referred to the same clinic who had received a diagnosis of probable dementia of the Alzheimer's type according to the criteria developed by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (McKhann et al., 1984). All subjects had a complete neurological examination and did not show any evidence of other neurological disease or other potential causes of dementia that could account for their condition. AD subjects were in an "early" stage of the disease and had a mean MMSE score of 22.1 (range: 17–25). Healthy elderly controls were 16 adults (10 females and 6 males) showing normal cognitive functioning, such as demonstrated by their performance on a general neuropsychological examination. Normal controls (NC) were matched to patient groups on the basis of age and educational level. Exclusion criteria for both the MCI, AD and healthy control subjects were a history of systemic or neurological disease (including cerebrovascular disease), past or current psychiatric illness, traumatic brain injury, history of alcoholism, untreated medical or metabolic condition, general anesthesia in the last 12 months, or uncorrected hearing and vision problems.

Demographic data of the three groups of patients indicate that they did not differ significantly in terms of age ($F(2,44) = 0.286$, $p = 0.752$; aMCI: mean (M) = 73.7, standard deviation (S.D.) = 6.3; AD: M = 74.2, S.D. = 6.5; NC: M = 72.4, S.D. = 7.1) nor education ($F(2,44) = 0.49$, $p = 0.615$; aMCI: M = 12.8, S.D. = 4.8; AD: M = 12.5, S.D. = 4.4; NC: M = 13.9, S.D. = 3.6). As expected, however, the three groups differed significantly in terms of their MMSE score ($F(2,44) = 38.2$, $p < 0.001$; aMCI: M = 27.4, S.D. = 1.6; AD: M = 22.1, S.D. = 2.9; NC: M = 28.1, S.D. = 1.5). Post-hoc analyses reveal a significant difference between AD and controls ($p < 0.001$) and between AD and aMCI ($p < 0.001$), but not between aMCI and controls ($p = 0.607$).

2.2. Neuropsychology

All three groups of participants underwent a comprehensive general neuropsychological evaluation, which included standard neuropsychological measures of memory, language, executive functions, visuospatial and visuoperceptual abilities. Episodic memory was assessed with the 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. Visual memory was assessed using the immediate and delayed recall (20 min) conditions of the Rey complex figure (Rey, 1960). Language was assessed using the 15-item version of the Boston Naming Test (Calero, Arnedo, Navarro, Ruiz-Pedrosa, & Carnero, 2002), as well as with the Letter (P) and Category (animals) fluency tests (Cardebat, Doyon, Puel, Goulet, & Joanette, 1990). Executive functions were assessed using the Stroop–Victoria test (Regard, 1981) and the Trail Making Test (Reitan, 1955). Short-term and working memory were evaluated using the forward and backward span subtests of the Weschler Memory Scale (Weschler, 2001). Visuoconstructional abilities were evaluated using the copy of the Rey–Osterrieth figure (Rey, 1960). Finally, the incomplete letters task of the Visual object and space perception battery (VOSP) (Warrington & James, 1991) was used to assess primary visuoperceptual processing and the Benton line orientation test was used to evaluate visuospatial abilities (Benton, Varney, & Hamsher, 1978).

2.3. Semantic memory test

This computerized task was devised by the principal investigator (S.J.) and was composed of two parts. The first part of the test evaluates the integrity of naming abilities and semantic memory of common generic concepts (objects), while the second part investigates the integrity of naming abilities and semantic memory of famous people.

(i) The first evaluation consisted of two parts. In the first part, subjects had to name and identify 40 photographs of objects, half of which were man-made objects and half of which were animals. First, a photograph of each object was presented individually on a computer screen and the subject was instructed to name the object. Once an answer had been provided, a series of four questions assessing semantic knowledge about the concept were presented one-by-one below the image. Each question assessed different concept attributes. For instance, the first question assessed categorical knowledge. Once an answer had been provided, a second question evaluating general perceptual knowledge of the object was presented. A third and fourth question evaluated functional/encyclopedic knowledge of the concept. Questions were formulated so that the subject had to provide yes/no responses. This semantic recognition task was intentionally chosen to reduce the load of controlled strategic retrieval processes required to access and manipulate semantic knowledge in memory. There were as many positive and false statements. Subjects were explicitly asked to answer the question based on the most widely culturally accepted answer and not on the basis of their own personal experiences, therefore relying on semantic-based information rather than on episodic-based information. A correct response was given if the subject was able to provide the specific name of the photograph that was presented. If a partial response was provided (for example, 'bear' for 'polar bear'), subjects were encouraged to provide a more specific response. Stimuli were presented randomly within each session using the E-Prime software (Psychology Software Tools, Pittsburg, PA).

(ii) The second part of the semantic memory test involved the presentation of 30 photographs of famous people, including local and international actors, politicians, athletes, singers, etc. One third of the celebrities were famous in the last 15 years (recent), another third were famous between 1970 and 1990, and one third was famous between 1930 and 1970. As in the first part, photographs of faces of famous people were presented one at a time on a computer screen. The subject first had to name the famous person. Once an answer had been provided, a series of questions assessing semantic knowledge about the person were presented one-by-one below the image. The first question concerned the nationality of the celebrity, the second question concerned his/her occupation, the third and fourth questions concerned specific biographical information about the individual, and the last question concerned the period during which the celebrity was famous. As in the first part of the test, questions were formulated so that the participant had to provide yes/no responses. There were as many positive and false statements and stimuli were presented randomly within each session. Again, subjects were explicitly asked to answer the question based on the most widely culturally accepted answer and not on the basis of their own personal experiences. Practise stimuli were presented before the beginning of each session. Again, a response was considered correct if the subject was able to provide the full name (first and last name) of the famous face that was presented. If a partial response was provided (for example, initials such as JFK or only the last name), the subjects were encouraged to provide the complete name.

During a subsequent evaluation that took place 2 weeks later, the exact same stimuli (objects and people) were presented from their names on the computer screen and spelled aloud at the same time by the experimenter. The purpose of this second evaluation was to examine if subjects accessed semantic knowledge about different classes of concepts differently in visual (i.e., photographs) vs. verbal (names) modalities. During this session, names were once again presented one-by-one, and subjects had to provide yes/no answers to the same questions described above (no naming was required during this session). This type of experimental design allows verifying the consistency of performance over different assessments. A consistent pattern of impairment across modalities is assumed to reflect central semantic impairments (e.g., Joubert et al., 2004, 2006). The outcome measure here is the proportion of correct responses for objects and famous people between the two administrations of each portion of the semantic memory test. The order of presentation was counterbalanced so that half of the participants underwent the objects test first and the other half underwent the test of famous people first. Again, stimuli were randomized within each part of the test. Photographs were always presented during the 1st evaluation while names were presented during the 2nd evaluation, so that verbal presentation of the names would not cue subsequent presentation of photographs which had to be named. A list of the stimuli is presented in Appendix A, as well as examples of the questions that were asked for objects and famous people.

2.4. Statistical analyses

2.4.1. Neuropsychological tests

One-way analyses of variance were carried out on the neuropsychological tests for the three groups of subjects. A Levene test was used to assess homogeneity of variances. When homogeneity of variance was met, significant main effects were analyzed using Tukey's honestly significant difference (HSD). If the homogeneity of variance was broken, the Welch F was used to determine significance and significant main effects were analyzed using Mann–Whitney U-tests.

2.4.2. Naming

The naming data were analyzed using separate two-way repeated measures analyses of variance on the percentage of correct responses. First, analyses of variance (ANOVA) were carried out on the data item-by-item. Single items were entered as the between-factor variable (objects, famous people) and stimulus category was the within factor (NC, aMCI, AD), which allows to consider the variance between single items in calculating the significance of an interaction. Second, analyses of variance with stimulus category as the within-factor, and group as the between-factor were carried out to confirm results from the item analyses of variance. Decomposition of significant interactions was carried out using the least significant differences (LSD) method. We used an alpha level of 0.05 for all statistical tests.

2.4.3. Task difficulty (naming)

A number of studies have addressed the question of task difficulty in the context of assessing semantic knowledge and naming of people and objects (Kay & Hanley, 2002; Lyons, Kay, Hanley, & Haslam, 2006; Miceli et al., 2000). Lyons et al. (2006) emphasized the importance of controlling for task difficulty when carrying out studies on category-specific differences: a test may be less sensitive than another because of possible differences in difficulty between the items, which may be due to high variability on one test and low variability on another. They suggested that one way to control item difficulty is to provide two tests of the same format in which means and standard deviations of control performance is carefully matched (Lyons et al., 2006). If we still observe differences between tests, then this would reinforce the finding of differences between two tests. We thus carried out a post-hoc analysis on the naming data. We selected 10 objects and 10 famous people that were matched for naming difficulty in our control subjects (80.6% correct naming). We then compared the naming performance for the same 10 objects and 10 famous faces in the MCI and in the AD groups. A two-way repeated measures ANOVA of naming performance was carried out. Post-hoc contrasts using LSD method were performed when necessary.

2.4.4. Semantic questions

The analyses of performance on tests of semantic knowledge of objects and famous people were identical to those of naming performance. Overall percentage of correct answers on semantic questions was determined using a composite score which was calculated by averaging performance across all semantic probes for each item.

2.4.5. Consistency between naming and semantic knowledge

Since the same items were used for object naming and semantic knowledge, one important question we wished to address was to examine if there was a consistency at the item specific level between naming performance and performance on semantic probes, in order to examine whether anomia in the aMCI and AD groups is associated with underlying semantic impairment. In order to do this, we examined naming and semantic performance between each subject at the item-by-item level. We examined the performance for each item across each subject, and determined the overall number of occurrences at the single item level when: naming and semantics was correct; naming and semantics was incorrect; naming was correct but semantics incorrect; and naming incorrect but semantics correct. We performed chi-square analyses on the data to determine if a significant association between naming and semantics was found.

2.4.6. Modality effects

In order to determine if the groups differed in terms of their ability to answer semantic probes in different modalities of presentation (visual and verbal), separate two-way repeated measures ANOVA with one within-factor, group (NC, aMCI, AD) and one between-factor, modality (visual and verbal) were carried out on the percentage of semantic questions answered correctly. An ANOVA was carried out one for the category of famous people, and another for the category of objects. Post-hoc contrasts were carried out using the LSD method. Finally, analyses of variance with stimulus category as the within-factor, and group as the between-factor were carried out to confirm these results.

2.4.7. Consistency between the visual and verbal modality

We examined if there was a consistency at the item-by-item level between semantic performance in the visual modality and in the verbal modality. In order to perform this, we examined semantic performance, in both modalities, at the item specific level and for each subject. We examined the performance for each single item across each subject, and determined the overall number of instances at the single item level when: visual and verbal semantics was correct; visual and verbal semantics was incorrect; visual semantics was correct but verbal semantics incorrect; and visual semantics was incorrect but verbal semantics correct. We then ran chi-square analyses on this data to determine if there was a significant association between semantic performance in the visual modality and in the verbal modality.

2.4.8. Post-hoc voxel-based morphometry analysis

The behavioral results revealed semantic deficits in both aMCI and AD patients. In order to map the regions responsible for this semantic deficit in our patient sample, we correlated the gray matter (GM) volume at a voxel level with the severity of the semantic deficit in our patient population using voxel-based morphometry. The semantic performance was represented by the mean Z score obtained in the four tests assessing semantics, i.e., semantic test of objects and people in both picture and verbal modality.

It has been recently proposed that semantic cognition is supported by a three-region neural network: bilateral anterior temporal regions, left prefrontal cortex and left temporo-parietal regions (Jefferies & Lambon Ralph, 2006). The anterior temporal lobe (ATL) region would represent an amodal semantic representation store, while the prefrontal and temporo-parietal regions would be involved in the 'semantic control', i.e., the executive-control mechanisms that interact with the semantic representation to produce an appropriate activation of key knowledge for a specific task. Based on this model, we expect to observe a significant correlation between GM integrity in ATL and semantic test performance if the semantic impairment is mainly due to a loss of conceptual representation, and in the prefrontal and temporo-parietal regions if the semantic impairment is determined by a deficit of semantic control.

Table 1
Neuropsychological data of controls, aMCI and AD patients.

	Controls Mean (S.D.)	aMCI Mean (S.D.)	AD Mean (S.D.)	p value for group effect
Memory				
RL/RI 16				
Immediate free recall of a word list (16)	10.9 (2.5)	6.7 (2.9)[b]	2.2 (2.0)[b,d]	$p < 0.001$
Immediate total recall of a word list (16)	14.8 (1.1)	13.7 (3.0)	7.1 (2.9)[b,d]	$p < 0.001$
Delayed free recall of a word list (16)	11.3 (2.3)	7.4 (4.1)[b]	1.9 (2.7)[b,d]	$p < 0.001$
Delayed total recall of a word list (16)	15.5 (0.7)	12.7 (2.8)[a]	6.4 (3.9)[b,d]	$p < 0.001$
Rey–Osterrieth immediate recall (36)	15.3 (5.6)	9.5 (4.9)[b]	4.7 (2.6)[b,c]	$p < 0.001$
Rey–Osterrieth delayed recall (36)	14.7 (6.1)	9.7 (4.5)[a]	4.4 (2.2)[b,d]	$p < 0.001$
Executive function/working memory				
Stroop–Victoria Test				
Part A	17.1 (4.0)	14.9 (4.9)	20.8 (5.9)[d]	$p < 0.01$
Part B	19.1 (4.6)	21.1 (4.9)	32.0 (14.7)[b,d]	$p < 0.01$
Part C (interference)	38.4 (15.8)	36.4 (9.1)	66.0 (36.9)[b,d]	$p < 0.01$
Trail Making Test				
Part A	45.8 (14.0)	48.2 (18.7)	74.9 (54.1)	ns
Part B	115.3 (41.7)	144(65.7)	257.9 (163.9)[b,c]	$p < 0.001$
Digit span forward	5.8 (0.8)	5.1 (1.5)	5.7 (1.4)	ns
Digit span backward	4.4 (1.1)	3.9 (1.6)	3.9 (0.7)	ns
Language				
Naming (Boston naming) (15)	13.0 (1.3)	12.1 (2.0)	10.9 (1.9)[b]	$p < 0.01$
Verbal fluency "P" in 2 min	22.6 (4.8)	20.8 (8.1)	14.9 (4.4)[b,d]	$p < 0.001$
Category fluency "animals" in 2 min	24.8 (7.4)	18.7 (4.6)[a]	15.1 (6.4)[b]	$p < 0.001$
Visual perception				
Visual object and space perception battery				
Incomplete letters (20)	19.6 (0.8)	18.8 (1.5)	18.6 (1.7)	ns
Rey–Osterrieth figure – copy (36)	31.9 (3.6)	28.9 (3.5)	27.9 (6.7)	ns
Benton line orientation (30)	21.1 (4.2)	21.3 (4.1)	21.2 (3.9)	ns

Results are presented in Mean and S.D. in brackets.
[a] $p < 0.05$ between control group and patient group.
[b] $p < 0.01$ between control group and patient group.
[c] $p < 0.05$ between MCI and AD groups.
[d] $p < 0.01$ between MCI and AD groups.

2.4.8.1. *Subjects.* All aMCI and AD subjects that participated in the behavioral study who were able to undergo a high-quality MRI scan were included in the imaging study. The scan was acquired within six months from neuropsychological testing. The group was composed of 25 patients. In the voxel-based morphometry correlation analysis all subjects were entered in the statistical analysis as a single group as previously described (Brambati et al., 2006; Rosen et al., 2005), and they were not sub-grouped on the basis of their diagnosis. However, for sample characterization purposes, the subject group included fourteen aMCI and eleven AD.

2.4.8.2. *Image acquisition.* MRI scans were obtained on a 3T Siemens Trio MRI (Siemens, Erlangen, Germany). High resolution anatomical images were acquired using an optimized MPRAGE protocol (TR = 2.3 s, TE = 2.94 ms, TI = 900 ms, flip angle = 9°, FOV = 256 × 240, voxel 1 mm × 1 mm × 1.2 mm) using an 8-channel coil. Images were acquired in the horizontal plane.

2.4.8.3. *Voxel-based morphometry analysis.* VBM analysis included image spatial pre-processing and statistical analysis. Both steps were implemented in the SPM2 software package (Wellcome Department of Imaging Neuroscience, London; http://www.fil.ion.ucl.ac.uk/spm) running on Matlab 6.5.1 (MathWorks, Natick, MA).

2.4.8.4. *Image pre-processing.* Anatomical MRI images were spatially pre-processed using standard procedures (Good et al., 2001). All T1 structural images were segmented, bias corrected and spatially normalized to Montreal Neurological Institute (MNI) space using the unified segmentation procedure (Ashburner & Friston, 2005). The VBM analysis was based on modulated gray matter images, whereby the gray matter value in each voxel is multiplied by the Jacobian determinant derived from the spatial normalization in order to preserve the total amount of gray matter from the original images. These modulated gray matter images were smoothed with a Gaussian kernel (12 mm FWHM).

2.4.8.5. *Statistical analysis.* The mean Z score in semantic tests was entered as covariate of interest in the 'covariate model'. Person and object semantic test scores were combined to achieve greater statistical power. Smoothed gray matter images of all subjects, irrespective of their diagnosis, were entered as a single group in the statistical model. Age and gender were entered as nuisance covariates. Global nuisance effect was accounted by scaling all images to the same global volume. The correlation was tested using a [1] *t*-contrast, assuming that decreased semantic abilities would be associated with decreased gray matter volumes.

The significance of each effect of interest was determined using the theory of Gaussian fields (Friston et al., 1994). When exploring all brain, a statistical threshold of $p < 0.05$ corrected for multiple comparisons (SPM family-wise error – FWE) was accepted. A less conservative threshold of $p < 0.005$ uncorrected was adopted in our regions of interest (ROIs) including bilateral temporal lobes, the prefrontal cortex and the temporo-parietal regions (Jefferies & Lambon Ralph, 2006).

3. Results

3.1. Neuropsychological tests

Results of the neuropsychological evaluation of the three groups of subjects and significant main effects are presented in Table 1. Results indicate that aMCI patients differ significantly from controls only on tests of verbal and visual episodic memory, confirming the isolated nature of the memory impairment in this group. Interestingly, the only other neuropsychological test for which aMCI patients were significantly more impaired than controls was the category fluency test. Category fluency may represent an early indicator of semantic decline in aMCI (Adlam et al., 2006; Hodges, Erzinclioglu, & Patterson, 2006; Murphy, Rich, & Troyer, 2006).

3.2. Naming

Results of the naming performance are presented in Fig. 1. A two-way repeated measures ANOVA of naming performance

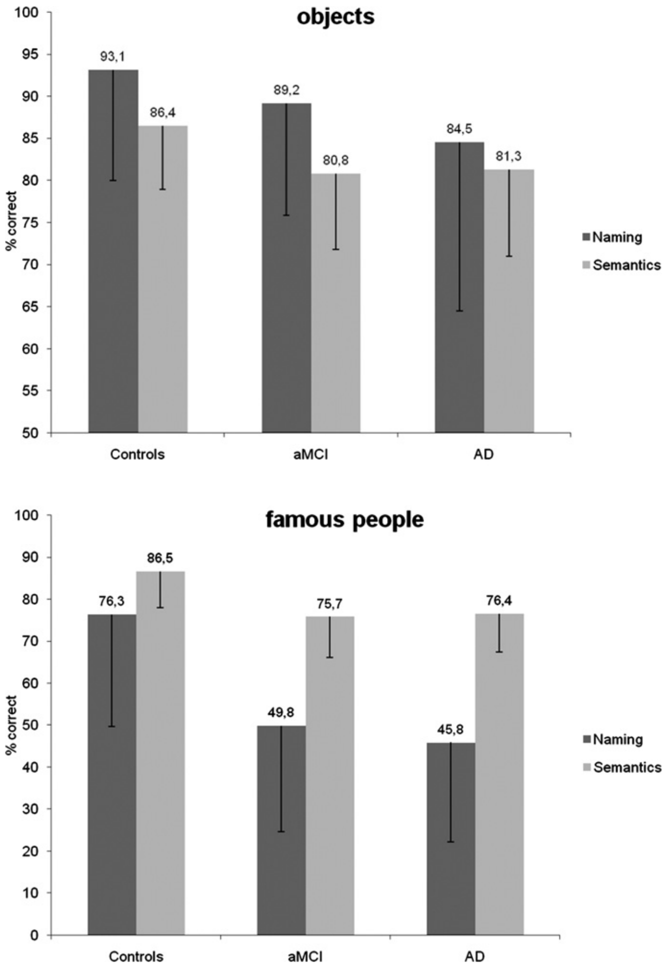

Fig. 1. Performance of control, aMCI and AD groups at naming and answering semantic questions from photographs.

performed on percentage correct responses revealed a significant stimulus category × group interaction ($F(2,136) = 30.92$, $p < 0.001$). Decomposition of this interaction showed a significant group effect for the objects test ($F(2,136) = 8.13$, $p < 0.001$) and for the famous people's test ($F(2,136) = 90.29$, $p < 0.001$). Post-hoc contrasts revealed that the aMCI and the AD groups were significantly more impaired than the control group at naming objects ($p = 0.023$ and $p < 0.001$, respectively) and famous faces ($p < 0.001$), but the aMCI and AD groups did not differ between each other. In addition, decomposition of the stimulus category × group interaction revealed a significant stimulus category effect. Post-hoc comparisons indicate that naming performance was significantly better for objects than for famous people in all three groups ($p < 0.001$). Finally, an ANOVA with stimulus category as the within-factor and group as the between-factor confirmed results of the item analysis. Taken together, results demonstrate that naming objects and famous people is impaired in both aMCI and AD groups when compared to controls, corroborating similar findings in the literature (Adlam et al., 2006; Joubert et al., 2008; Thompson et al., 2002).

3.2.1. Task difficulty

We selected 10 objects and 10 famous people that were matched for naming difficulty in our control subjects (80.6% correct naming). Mean naming performance was 80.7% for objects and 47.3% for famous people in the MCI group, and 70.6% for objects and 46.3% for famous people in the AD group. The aMCI group and the AD group were significantly impaired at naming famous faces when compared to the control group ($p < 0.001$), but the aMCI and AD groups did not differ between each other. The aMCI and AD groups were not significantly impaired at naming objects relative to controls. Moreover, a significant stimulus category effect was found: famous face naming was significantly more impaired than naming objects in the aMCI group ($F(1,18) = 25.06$, $p < 0.001$) and in the AD group ($F(1,18) = 6.52$, $p < 0.05$). Subject analyses overall confirmed these results. In conclusion, even when object and famous face naming performance is strictly controlled for difficulty in healthy subjects, naming famous faces remains significantly more affected than naming objects in aMCI and early AD, suggesting that differences between these categories of knowledge are not due to task difficulty. With respect to semantic performance in control subjects, performance was identical for objects and people (objects: 86.4% and people: 86.5%, see Fig. 1), indicating that semantic questions were equivalent in terms of difficulty.

Table 2A
Number of observed values at the item specific level for naming and semantic performance in the aMCI and AD groups. Chi-square tests indicate the significant naming-semantic associations.

	Semantic knowledge					
	aMCI[a]			AD[b]		
	Correct	Incorrect	Total	Correct	Incorrect	Total
Famous people						
Correct	90	14	104	84	136	220
Incorrect	134	212	346	50	210	260
Total	224	226	450	134	346	480
Objects						
Correct	208	316	524	249	292	541
Incorrect	25	51	76	39	60	99
Total	233	367	600	288	352	640

[a] $\chi^2(1) = 73.1$, $p < 0.001$; $\chi^2(1) = 1.29$, $p = 0.26$.
[b] $\chi^2(1) = 21.27$, $p = 0.001$; $\chi^2(1) = 1.49$, $p = 0.22$.

3.3. Semantic questions

Analysis of semantic performance expressed in percentage correct response revealed a significant stimulus category × group interaction ($F(2,136) = 6.56$, $p = 0.002$). Decomposition of this interaction showed a significant group effect for the objects test ($F(2,136) = 18.65$, $p < 0.001$) and for the famous persons test ($F(2,136) = 51.40$, $p < 0.001$). Post-hoc contrasts (LSD) showed that for object semantics, the control group performed better than the aMCI group ($p < 0.001$) and the AD group ($p < 0.001$), but that the aMCI group did not differ from the AD group. With respect to person semantics, the aMCI and the AD groups both differed significantly from the control group ($p < 0.001$) but again the aMCI did not differ significantly from the AD group. An ANOVA with stimulus category as the within-factor and group as the between-factor replicated these results. Moreover, a significant stimulus category effect was found. Post-hoc comparisons showed that semantic knowledge of famous people was significantly more impaired than knowledge of objects in both the aMCI and AD groups ($p = 0.028$ and $p = 0.044$, respectively), but not in the control group. In sum, these analyses show that semantic knowledge for objects and famous people is impaired in both aMCI and AD groups when compared to controls, but that famous people knowledge is significantly more affected than object knowledge (see Fig. 1).

3.4. Consistency between naming and semantic knowledge

Results are presented in detail in Table 2A. A very significant association between naming and semantic knowledge for famous people was found in the aMCI group ($\chi^2(1) = 73.1$, $p < 0.001$) and in the AD group ($\chi^2(1) = 21.27$, $p < 0.001$). However, no significant association between naming and semantic knowledge for objects

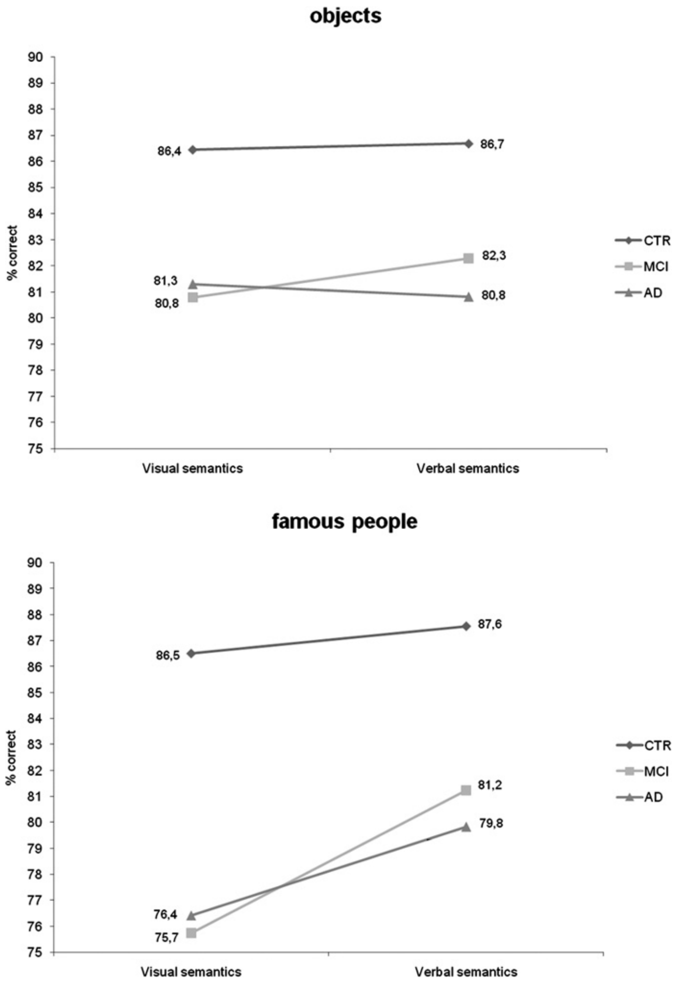

Fig. 2. Performance of controls, aMCI and AD groups in the visual and verbal modalities of the semantic test.

was found in the aMCI group ($\chi^2(1) = 1.29$, $p = 0.26$) and in the AD group ($\chi^2(1) = 1.49$, $p = 0.22$).

3.5. Modality effects

Results are illustrated in Fig. 2. An ANOVA for famous people knowledge showed a significant modality × group interaction ($F(2,58) = 7.31$, $p < 0.001$). Decomposition of this interaction showed a significant group effect both for the visual ($F(2,58) = 40.06$, $p < 0.001$) and the verbal modalities ($F(2,58) = 23.53$, $p < 0.001$). Post-hoc analyses demonstrated that the aMCI and the AD groups were more impaired than the control group ($p < 0.001$) in both the visual and in the verbal modality. The aMCI and AD groups did not differ between each other in either modality. Decomposition of the group by modality interaction also showed a modality effect for the aMCI group ($F(1,59) = 15.80$, $p < 0.001$) and for the AD group ($F(1,59) = 8.97$, $p = 0.006$) but not for the control group ($F(1,59) = 0.93$, $p = 0.342$), indicating that semantic knowledge of famous people was more impaired in the visual than in the verbal modality in aMCI and AD patients. Results of the ANOVA for objects demonstrated no significant modality by group interaction ($F(2,78) = 1.67$, $p = 0.19$). There was an absence of modality effect ($F(2,78) = 0.37$, $p = 0.55$), although a group effect was found ($F(2,78) = 32.19$, $p < 0.001$). Post-hoc contrasts showed that the aMCI and the AD groups were more impaired than the control group in terms of object knowledge ($p < 0.001$). Analyses of variance using individual subjects as cases analyses replicated these results. In sum, semantic knowledge of objects and famous people is impaired in both the visual and verbal modality in aMCI and AD. Knowledge of famous people is more impaired in the visual than in the verbal modality in these patients, while knowledge of objects is similarly affected in both modalities.

Table 2B
Number of observed values at the item specific level for semantic performance in the visual and in the verbal modalities in the aMCI and AD groups.

	Auditory-verbal					
	aMCI[a]			AD[b]		
	Correct	Incorrect	Total	Correct	Incorrect	Total
Famous people						
Correct	89	41	130	87	47	134
Incorrect	65	255	320	67	279	346
Total	154	296	450	154	326	480
Objects						
Correct	153	80	236	192	96	288
Incorrect	83	284	367	80	272	352
Total	236	364	600	272	368	640

[a] $\chi^2(1) = 95.21$, $p < 0.001$; $\chi^2(1) = 109.86$, $p < 0.001$.
[b] $\chi^2(1) = 90.02$, $p < 0.001$; $\chi^2(1) = 125.14$, $p < 0.001$.

3.6. Consistency between visual and verbal modalities

Results are presented in detail in Table 2B. With respect to the aMCI group, results indicate that there was a very significant association between semantic knowledge in the visual and in the verbal modalities for famous people ($\chi^2(1) = 95,21$, $p < 0.001$) and for objects ($\chi^2(1) = 109.86$, $p < 0.001$). A very significant association between semantic knowledge in the visual and in the verbal modalities for famous people was also found in the AD group ($\chi^2(1) = 92.02$, $p < 0.001$) and for objects ($\chi^2(1) = 125.14$, $p < 0.001$).

3.7. Neuroimaging results

No voxels showed significant correlation between the mean Z score and the GM volume when a threshold of $p < 0.05$ corrected for multiple comparisons (SPM family-wise error – FWE) was used. However, when the threshold was lowered to the more permissive threshold of $p < 0.005$ uncorrected in our ROIs based on previous studies (Jefferies & Lambon Ralph, 2006), the VBM correlation analysis revealed a significant positive correlation between semantic test performance and GM volume in the left anterior temporal lobe ($x = -49$, $y = 14$, $z = -26$, Z score = 2.8, $p < 0.005$ uncorrected, cluster size = 91 voxels) and in the left inferior prefrontal gyrus, pars opercularis (BA 44) ($x = -45$, $y = 12$, $z = 9$, Z score = 2.9, $p < 0.002$ uncorrected, cluster size = 92 voxels). No significant correlation was revealed in the temporo-parietal regions even when the threshold was lowered to $p < 0.05$ uncorrected (see Fig. 3). The removal of the AD patients from the analysis did not eliminate the positive correlation between semantic test performance and GM volume in the left anterior temporal lobe and in the left inferior prefrontal gyrus, pars opercularis (BA 44); in fact the positive correlation persisted in the MCI group, albeit with a predictably slightly lower level of significance (left ATL: Z score = 2.7, $p < 0.005$, left IFG: Z score = 2.5, $p = 0.007$).

4. Discussion

4.1. Naming

Our first objective was to evaluate aMCI subjects' confrontation naming abilities. Naming objects and naming famous faces were both significantly impaired in aMCI and AD patients. Consistent with previous findings (Ahmed et al., 2008; Joubert et al., 2008), naming famous faces was disproportionately impaired relative to

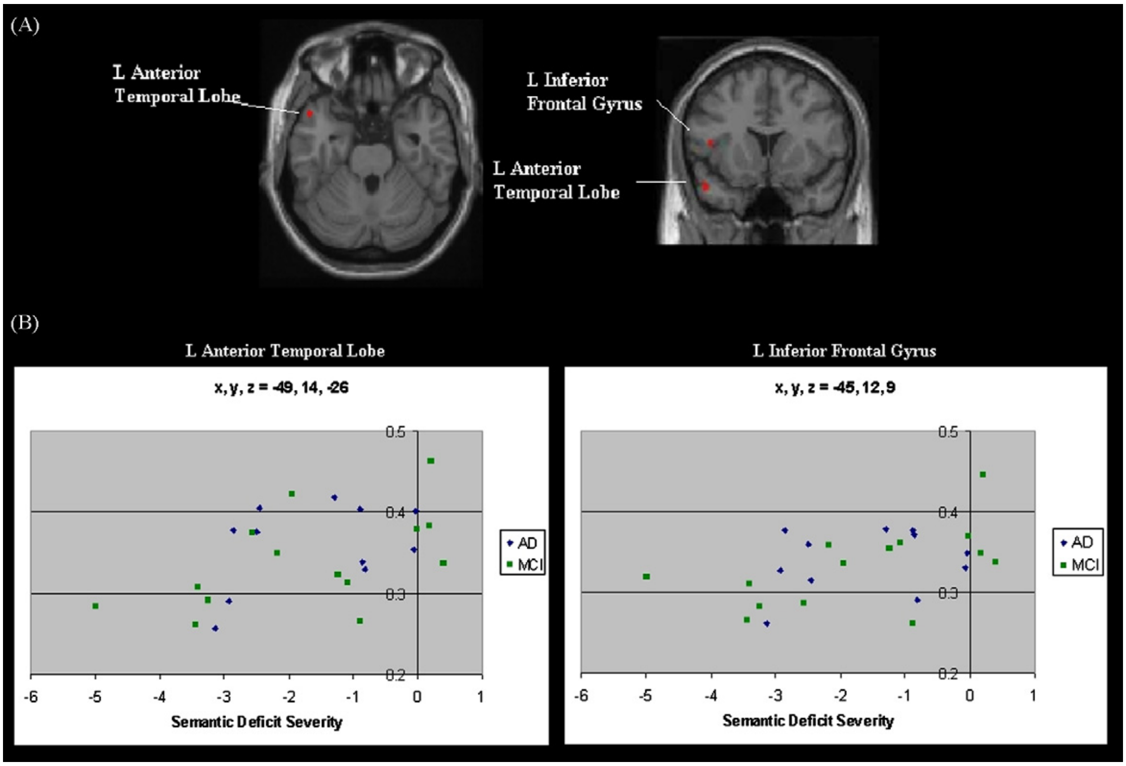

Fig. 3. (A) Brain areas in which the GM volume positively correlate with performance on the semantic tests. The threshold for display is $p < 0.005$, uncorrected. Maps of significant correlation are superimposed on axial and coronal sections of the canonical template of SPM2. (B) Relationships between gray matter volumes in arbitrary units (*y*-axis) and semantic deficit severity at the peak voxel.

naming objects in both groups (see Fig. 1). These findings suggest that confrontation naming tests in which pictures of objects are required to be named may be less sensitive diagnostic measures of anomia in aMCI than tests that require naming famous faces. Moreover, it is particularly important to investigate face naming abilities since they are a sensitive predictor of future conversion to AD (Estevez-Gonzalez et al., 2004; Thompson et al., 2002; Vogel et al., 2005). We also showed that this difference in the ability to name famous faces and objects in aMCI and AD is not due to the inherently more difficult nature of the former task. In fact, the difference was still present even when task difficulty was controlled for, following the method proposed by Lyons and colleagues (Lyons et al., 2006). Altogether, these results highlight the importance of including a famous persons naming task in the screening neuropsychological battery administered to aMCI patients.

4.2. Semantic memory

In addition to the naming impairment, aMCI and early AD patients showed impaired semantic knowledge of objects and famous people. With respect to previous studies which have focused on naming abilities, the present finding represents a significant step forward in understanding the nature of the memory impairment in very early AD. In addition, previous studies have not show whether naming difficulties in aMCI are associated with a breakdown of underlying semantic knowledge. In one seminal study by Chertkow and Bub (1990), the authors demonstrated that there was a strict correspondence in AD between naming impairment and impaired knowledge of the items that had to be named, suggesting that word finding difficulties were at least in part due to underlying semantic disruption. Here we tested whether the naming deficits observed in aMCI were associated with deficits in the semantic knowledge of the concept that had to be named. Our hypothesis that naming deficits in aMCI were associated with deficits in semantic memory was partly confirmed. We found that naming deficits were associated with underlying semantic deficits in aMCI and AD patients only for the category of famous people. In contrast, the association between naming and semantic knowledge of objects was not significant. A closer examination of naming and semantic knowledge of objects presented in Fig. 2A indicates that there were more occurrences of correct–incorrect naming-semantic associations, relative to the number of occurrences of incorrect–incorrect and correct–correct naming-semantic associations. This imbalance in the proportion of naming-semantic errors led to the absence of significant association between naming and knowledge of objects. One possible interpretation of these findings is that the mild semantic decline for objects in aMCI and in early AD may not be sufficient to compromise access to the lexical representations of objects. Because the lexical representations of objects are more generic, as opposed to the lexical representations of names which are unique and denote single individuals, lexical representations of objects may be more robust and may require a higher threshold of semantic impairment before they become affected.

Results concerning semantic knowledge of objects vs. famous people also offer interesting insights into the nature of the semantic impairment in aMCI and early AD. Contrary to a previous study in which we used free recall tasks to tap semantic knowledge about objects and people in aMCI patients (Joubert et al., 2008), the current study intentionally used semantic questions that provide maximal contextual information in order to reduce the load of effortful retrieval processes. It was found using this type of material that although object and famous person knowledge were both significantly impaired in aMCI and AD relative to controls, famous person knowledge was disproportionately affected relative to object knowledge in both aMCI and AD. In relation to our previous study, these results indicate that famous person knowledge is more impaired than object knowledge not only in naming and free recall tests, but also in low effortful semantic recognition tasks. Knowledge of famous people, which relies to a greater extent upon unique idiosyncratic information, may be more greatly affected than knowledge of objects in aMCI and AD, objects sharing more common attributes with other exemplars of their category and relying to a greater extent upon their sensory and functional properties (i.e., greater reliance upon sensory experience).

An argument in favor of the central nature of the semantic impairment in aMCI is the multimodal nature of the deficits that is observed. Subjects were asked identical semantic questions in different modalities two weeks apart, in the visual modality during the first session and verbal during the second. Object and person semantics were significantly impaired in both modalities in aMCI and AD patients, and item-by-item analyses showed that there was a highly significant correspondence between items in the visual and verbal modalities. Results of the present study corroborate in aMCI findings of previous studies which have evidenced impaired access to semantic knowledge from different modalities of input in different patient populations such as AD (Greene & Hodges, 1996) and SD (Snowden, Thompson, & Neary, 2004). An interesting finding is that person semantics was notably more affected in the visual than in the verbal modality in the aMCI and AD patients (see Fig. 2). One possible interpretation is that in addition to the semantic impairment, aMCI and early AD patients may also suffer from mild visuoperceptual face processing deficits which may exacerbate the semantic deficit in the visual modality. The perceptual analysis of complex visual stimuli such as faces may be impaired although this deficit may not be serious enough to affect visual object perception. In contrast, normal controls did not present with this pattern of performance. There is also an alternative interpretation to these results, proposed by Haslam and colleagues (Haslam, Kay, Hanley, & Lyons, 2004; Lyons et al., 2006). They found that young and elderly healthy subjects were more familiar with and produced more accurate information in response to the names of famous people than in response to their faces. The authors suggested that "faces and other visual information about people may simply be less stable than names" (Haslam et al., 2004, p. 462). In other words, changes in the appearance of faces may arise with age (such as changes in hairstyle, facial appearance, etc.), while names remain unchanged. These changes may confer greater vulnerability to faces than names.

Moreover, tasks requiring effortful, strategic access to semantic memory have been found to be altered in elders with aMCI (Duong et al., 2006). The questions assessing the semantic properties of concepts in our experimental procedure were intentionally presented in a recognition task, in an effort to reduce the executive load or the processes involved in the retrieval of semantic information required in free recall tasks. Subjects had to answer yes or no to questions that offered semantic contextual information, which did not require much effort in terms of retrieval, selection among competing semantic alternatives, and manipulation of semantic information. Therefore, we believe the semantic deficits observed in our aMCI and AD patients cannot be attributed solely to semantically oriented executive deficits. Rather, our results suggest that a deficit at the level of the representation of the concept is responsible for the deficits observed in semantic testing in aMCI and early AD, and that this central deficit may be combined with additional difficulties in the selection, manipulation and retrieval of knowledge.

4.3. Neural correlates of semantic impairment

Semantic cognition most likely relies upon a network of cortical regions including the ATLs, the left inferior prefrontal cortex, and temporo-parietal regions (Jefferies & Lambon Ralph, 2006). The aim of our VBM study was to investigate if the semantic impairment observed in our aMCI and early AD patients correlated with atrophy in this semantic network of regions underlying semantic cognition. Results first show that the degree of gray matter volume in the left ATL and in the left inferior frontal gyrus correlates with the performance in the semantic tests in aMCI and AD. Regarding the role of the ATL, several independent lines of evidence suggest that the ATL plays a critical role in the representation of an amodal semantic store (Patterson, Nestor, & Rogers, 2007). Evidence of the role of the ATL region in semantic memory has come in large part from the study of SD patients (Patterson et al., 2007). SD patients present with a progressive cross-modal semantic memory impairment along with atrophy predominating in the left inferior and anterior lateral temporal lobe (Hodges, Salmon, & Butters, 1992). There is also evidence to suggest that the ATL is more involved in processing concepts at a subordinate level rather than at a more general superordinate level (Rogers et al., 2006). Moreover, the integrity of the ATL region correlates with the integrity of semantic abilities (Brambati et al., 2006). Thus, the ATL has been described as key region in the semantic processing of concepts at a subordinate, abstract and amodal level (Patterson et al., 2007). Furthermore, converging evidence of the role of the ATL in conceptual knowledge has come from functional neuroimaging studies. In fact, an area of the left ATL almost overlapping with the one found in our study ($x = -50$, $y = 8$, $z = -22$) was found to be a common area of activation for the fine-grained semantic processing of objects and famous people (Gorno-Tempini & Price, 2001; Rogers et al., 2006). In summary, our results thus show that the performance in semantic tests in our patient sample is associated with the GM volume in left ATL structures. These neuroanatomical results also provide further evidence that a semantic control or access deficit alone cannot explain the semantic deficit observed in aMCI and early AD and that the observed semantic impairment is at least in part due to a breakdown of stored conceptual knowledge.

The semantic test performance in aMCI and AD also correlated with the GM volume in the left prefrontal cortex (IPC) at the level of the inferior frontal gyrus. This area has been previously associated with the control mechanisms that interact with the semantic representation to produce an appropriate activation of key knowledge in order to successfully achieve a semantic task (Jefferies & Lambon Ralph, 2006). Many fMRI studies have in fact demonstrated the involvement of this area during tasks requiring control of semantic information (Garavan, Ross, Li, & Stein, 2000; Peers et al., 2005). Other neuroimaging studies have identified the anterior and inferior prefrontal region as playing a key role in retrieving, maintaining, monitoring and manipulating conceptual representations distributed in other regions of the brain (Gabrieli, Poldrack, & Desmond, 1998; Martin & Chao, 2001; Poldrack et al., 1999). Even though in the present study we tried to reduce the involvement of executive mechanisms in the semantic task by presenting yes–no type questions in a recognition mode, our task may still have required to some degree the active generation and retrieval of semantic knowledge, which is compatible with atrophy found in the IPC in our patient sample. Finally, no significant correlation was found between semantic test performance and the GM volume in the temporo-parietal region, a region which has also been assumed to be associated with the semantic cognition network, even when the threshold was lowered to a very permissive level ($p < 0.05$ uncorrected). In conclusion, this study is the first to provide evidence that the integrity of the ATL and the IPC correlates with scores of semantic abilities of objects and people in aMCI and early AD.

4.4. Semantic memory in normal vs. pathological aging

Semantic memory does not have the same trajectory of decline in normal aging as other memory systems such as episodic memory and working memory. In normal aging, the most robust and well-documented age-related memory decline concerns episodic memory (Verhaeghen & Cerella, 2002; Verhaeghen & Marcoen, 1993; Wechsler, 1997), while accumulated semantic knowledge remains stable or even improves throughout the lifespan (Allen, Sliwinski, & Bowie, 2002; Allen, Sliwinski, Bowie, & Madden, 2002; Hoyer & Verhaeghen, 2006; Smith, 1996). In contrast, our results and those of previous studies indicate that semantic deficits may present as a very early manifestation of cognitive decline in incipient AD. Amieva et al. (2008) showed that the first measurable decline in cognitive performance began as early as 12 years before the development of dementia and was observed on a category fluency task, which is strongly associated with semantic knowledge. Predementia patients who later on developed AD were also at the outset more impaired at naming famous faces relative to the non-converters (Estevez-Gonzalez et al., 2004; Thompson et al., 2002; Vogel et al., 2005). Semantic tests may thus help discriminate pathological from normal ageing. Semantic deficits may often go unnoticed and this may be due in part to their mild nature and to the limited availability of clinically oriented semantic tests in a clinical setting. Future longitudinal studies are needed to determine if aMCI individuals presenting with semantic deficits are at greater future risk of converting toward AD and if semantic tests may contribute to improving early clinical diagnosis of AD.

5. Conclusion

This study demonstrated that aMCI patients present with naming deficits, as well as a genuine semantic impairment concerning objects and famous people. The pattern of semantic decline in MCI is similar to that found in early AD but contrasts with that found in normal aging. Semantic impairment was associated with distinct patterns of cortical atrophy in the ATL region previously documented to be affected in SD and activated in semantic related paradigms in neuroimaging studies (Rogers, 2006), as well as in the left IPC. Results of this study support the view that semantic impairment in aMCI and early AD may result from degraded semantic representations combined with selective deficits in the selection, manipulation and retrieval of semantic information.

Acknowledgements

This work was supported by a grant from the Alzheimer Society of Canada (ASC) to SJ and by a Chercheur-Boursier Junior 1 award to SJ. We are very thankful to statistician Francine Giroux for her valuable help with analyses and for very useful suggestions, and to Annie Dugas for her help in recruiting patient populations. We would also like to thank all the patients and control subjects who participated in this study.

Appendix A.

List of the stimuli that were used in the semantic memory test

Objects

Aspirateur (vacuum cleaner)
Chameau (camel)
Chat (cat)
Cheval (horse)
Chien (dog)
Ciseaux (scissors)
Clarinette (clarinet)
Eléphant (elephant)
Fusil (rifle)
Giraffe (giraffe)
Grenouille (frog)
Hache (axe)
Harmonica (harmonica)
Kangourou (kangaroo)
Lapin (rabbit)
Lion (lion)
Marteau (hammer)
Mètre de mesure (tape measure)
Mouton (sheep)
Ours Polaire (polar bear)
Papillon (butterfly)
Pelle (shovel)
Perceuse (drill)
Piano (piano)
Rasoir électrique (electric razor)
Rhinocéros (rhinoceros)
Saxophone (saxophone)
Scie (saw)
Sèche-cheveux (hair dryer)
Serpent (snake)
Singe (monkey)
Tigre (tiger)
Tire-bouchon (corkscrew)
Tondeuse à Gazon (lawnmower)
Tortue (turtle)
Tournevis (screwdriver)
Trompette (trumpet)
Tronçonneuse (chainsaw)
Vache (cow)
Zèbre (zebra)

Famous people

Albert Einstein
Alfred Hitchcock
Arnold Schwarzenegger
Camillien Houde
Catherine Deneuve
Céline Dion
Charles Aznavour
Charlie Chaplin
Elvis Presley
George Bush
Gilles Vigneault
Ginette Reno
Guy Lafleur
Jean Chrétien
Jean Drapeau
Jean Lesage
Jean-Paul II
John F. Kennedy
John Wayne
Louis de Funès
Marlène Dietrich
Marylin Monroe
Maurice Duplessis
Maurice Richard
Michael Jackson
Pierre Elliott Trudeau
Reine Elizabeth II
René Lévesque
Robert Charlebois
Wayne Gretzky

Examples of questions that were used in the semantic memory test (verbal modality)

Objects

Tortue (turtle)
- Est-ce que c'est un animal qui vit dans l'Arctique? (Is this an arctic animal?)
- Est-ce que ça a un bec? (Does this animal have a beak?)
- Est-ce que ça peut vivre dans l'eau? (Can this animal live in the water?)
- Est-ce que ça saute? (Can this animal jump?)

Mouton (sheep)
- Est-ce que c'est un animal sauvage? (Is it a wild animal?)
- Est-ce que ça a des griffes? (Does this animal have claws?)
- Est-ce que ça produit du fromage? (Can you produce cheese from this animal?)
- Est-ce que ça se mange? (Can you eat the meat from this animal?)

Scie (saw)
- Est-ce que c'est un instrument de jardinage? (Is this and instrument that is used for gardening?)
- Est-ce qu'il y en a qui sont rondes? (Is it round-shaped?)
- Est-ce qu'il y en a qui font de la musique? (Can it be used to play music?)

Est-ce qu'il y en a qui s'utilisent à deux personnes? (Can it be used by two persons?)

Famous people

Camillien Houde

Est-ce que cette personne est un homme politique? (Was this person a politician?)
Est-ce que cette personne est américaine? (Is this person American?)
Est-ce que cet homme a été Premier Ministre du Canada? (Was this person Prime Minister of Canada?)
Est-ce qu'il était apprécié par les Montréalais? (Was this person appreciated by Montrealers?)
Est-ce que cette personne a été au pouvoir dans les années 40? (Was this person in power in the 1940s?)

Celine Dion

Est-ce que cette personne est une chanteuse? (Is this person a singer?)
Est-ce que cette personne est originaire de France? (Is this person native from France?)
Est-ce que son mari était son imprésario? (Was her husband her impresario?)
Est-ce qu'elle est enfant unique? (Was she a single child?)
Est-ce que cette personne est devenue connue dans les années 60? (Did this person become famous in the 1960s?)

Marylin Monroe

Est-ce que cette personne est une danseuse? (Is this person a dancer?)
Est-ce que cette personne est américaine? (Is this person American?)
Est-ce que cette femme décédée dans un accident de voiture? (Did this woman die in a car accident?)
Est-ce qu'elle a eu une histoire d'amour avec le Président des États-Unis? (Did she have an affair with the President of the United States?)
Est-ce que cette personne était très connue dans les années 80? (Was this person very famous in the 1980s?)

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