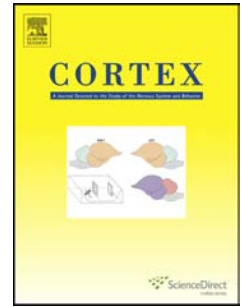


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Cognitive and neuroimaging evidence of impaired interaction between self and memory in Alzheimer's disease

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**Running title:** self-related memory in Alzheimer disease

**Key words:** Self-reference effect; memory; recollection; Alzheimer's disease; fMRI.

### Abstract

In human cognition, self and memory processes strongly interact, as evidenced by the memory advantage for self-referential materials (*Self Reference Effect* (SRE) and *Self Reference Recollection Effect* (SRRE)). The current study examined this interaction at the behavioural level and its neural correlates in patients with Alzheimer's disease (AD). Healthy older controls (HC) and AD patients performed trait-adjectives judgements either for self-relevance or for other-relevance (encoding phase). In a first experiment, the encoding and subsequent yes-no recognition phases were administered in an MRI scanner. Brain activation as measured by fMRI was examined during self-relevance judgements and anatomical images were used to search for correlation between the memory advantage for self-related items and grey matter density (GMD). In a second experiment, participants described the retrieval experience that had driven their recognition decisions (familiarity vs. recollective experience). The behavioural results revealed that the SRE and SRRE were impaired in AD patients compared to HC participants. Furthermore, verbal reports revealed that the retrieval of self-related information was preferentially associated with the retrieval of contextual details, such as source memory in the HC participants, but less so in the AD patients. Our imaging findings revealed that both groups activated the medial prefrontal cortex (MPFC) at encoding during self-relevance judgments. However, the variable and limited memory advantage for self-related information was associated with GMD in the lateral prefrontal cortex in the AD patients, a region supporting high-order processes linking self and memory. These findings suggest that even if AD patients engage MPFC during self-referential judgments, the retrieval of self-related memories is qualitatively and quantitatively impaired in relation with altered high-order processes in the lateral PFC.

## I. Introduction

The concept of self has received much attention during the last decade. Current theoretical views suggest that despite a phenomenal appearance of unity, the self is actually made of several components. According to Klein & Gangi (2010), the self is formed by different, functionally isolable components including, notably, episodic memories of one's life events and semantic summary representations of one's personality traits. The multiplicity of functionally isolable cognitive components implies that the self might be supported by several brain regions each specialised in one aspect and that some aspects of the self may be preserved while others are impaired in neurocognitive pathologies (Klein & Gangi, 2010; Martinelli et al, in press). In this view, Damasio (1999; see also Northoff et al., 2006) distinguished three main systems: the "proto self" that refers to a "bodily-self", the "core self" which supports the discrimination of self-related stimuli from self-unrelated stimuli, and the "autobiographical self" which reflects the linkage of self-referential stimuli to the memory domain. The "core-self" is supramodal and receive afferent connections from all sensory modalities. It allows for an active and explicit distinction between self and non-self-related intero- and exteroceptive stimuli. In contrast, the "autobiographical self" is related to high-order cognitive processes. Actually, the authors proposed that the core self filters, selects, and provides those stimuli that are relevant for a particular person's self. Only self-related stimuli are then elaborated further by higher-order processing (i.e., in the autobiographical self). The interaction between the self and memory has also been conceptualised in the Self-Memory System (SMS; Conway and Pleydell-Pearce, 2000; Conway, 2005). The SMS contains two main components: *the working self* and *the autobiographical knowledge base*. The working self refers to control processes based on currently active goals. This executive component

manages the encoding and controlled retrieval of information in and from the autobiographical knowledge base.

Strong evidence for the interaction between self and long-term memory can be found in studies using laboratory self-referential materials. Indeed, in these studies, retrieval performance is better for information that has been encoded in reference to the self than for information that has been processed semantically or in reference to other people. This well-known cognitive phenomenon, named the Self Reference Effect (SRE; Rogers et al., 1977), is a strong characteristic of human cognition since it has been observed in various populations including healthy older people (Gutchess et al., 2007), with various materials and various paradigms at encoding and recognition and with different designs (for a review see Symons and Johnson, 1997).

This interaction between self and long-term memory seems to be mediated by complex cognitive mechanisms. Self-reference at encoding may promote elaborate and organized processing, leading to a memory representation having item-specific and relational information (Symons & Johnson, 1997; Klein, 2012). At retrieval, such deeply encoded information would promote recollection (i.e. controlled and conscious episodic retrieval of information together with the context and elaborations from encoding (Tulving, 2002) rather than familiarity (i.e. a relatively automatic process of global assessment of memory strength or stimulus fluency (for reviews, see Yonelinas, 2002 and Yonelinas et al., 2010)). In support of this hypothesis, several authors have shown that the retrieval of information associated to the self is more likely to be associated with a recollection-based retrieval as reflected by recollective experience (as assessed by the Remember/Know procedure (Tulving, 1985; Gardiner, 1988)) and source memory (Conway & Dewhurst, 1995; Conway et al., 2001;

Carroll et al., 2001; Van den Bos et al., 2010). This phenomenon, termed the Self Reference Recollection Effect (SRRE, Conway et al., 2001), suggests that recollection-based processes support episodic retrieval of information that has been previously associated to the self.

Alzheimer's disease (AD) is characterized by impaired recollection-based processes, such as controlled retrieval (Knight, 1998; Smith and Knight, 2002; Adam et al., 2005; Genon, Collette, Feyers et al., 2013) and experience of remembering (Dalla Barba, 1997; Rauchs et al., 2007). In the same line, the quality of the recollective experience for autobiographical memories is impaired in AD patients (Irish, Hornberger, et al., 2011; Irish, Lawlor, et al., 2011; Piolino et al., 2003). In particular, AD patients are impaired across a range of behavioural characteristics inherent to recollective experience, such as self-referential imagery, vividness and retrieval of contextual details (Irish, Hornberger, et al., 2011; Irish, Lawlor, et al., 2011). In summary, these findings suggest that most aspects of recollection-based retrieval, i.e. episodic retrieval, are impaired in AD patients.

In this context, if the retrieval of self-referential information is primarily supported by recollection-related processes (i.e. episodic retrieval), one may assume that it is impaired in AD. More precisely, the impairment of the recollective experience in AD may lead to poor retrieval of self-referential information at the quantitative and qualitative levels, so that patients do not benefit from encoding information in reference to themselves. In other words, one may expect the SRRE and SRE, i.e. interaction between self and memory, to be altered in AD patients. To our knowledge, three studies have investigated the SRE and the SRRE in AD patients. The results of these studies suggest that SRE and SRRE, at the group level, may be relatively preserved when driven by emotional material in AD patients (Lalanne et al., 2010; Kalenzaga, Bugańska et al., in press; Kalenzaga and Clarys, in press). Thus, self-reference

may, in some cases, promote relational encoding and therefore recollection-based processes at retrieval, in particular, retrieval of contextual details (Carroll et al., 2001) in AD patients. However, to our knowledge, the quality of retrieval experience has never been rigorously examined in AD patients for information encoded in reference to the self.

In healthy young populations, judgments about the self are known to engage cortical midline structures such as the medial prefrontal cortex (MPC; D'Argembeau et al., 2005; D'Argembeau et al., 2007; for a review see Northoff et al., 2006). According to Northoff et al. (2006), the ventral part of the MPFC discriminates self-related stimuli from self-unrelated stimuli, hence supporting the core self. As stated above, this self-referential processing filters, selects, and provides those stimuli which are relevant for a particular person's self. Some studies investigated the neural correlates of this self-referential processing (i.e. the core self) in MCI and AD patients and suggested that, in many conditions, patients' brain functioning was modified during this process (Ruby et al., 2009; Zamboni et al., 2012). The core self might thus be altered in AD patients.

According to Northoff et al. (2006), only self-referential stimuli (selected by the core self) are elaborated further in higher-order processing, such as autobiographical memory/self. Considering that lateral frontal regions (such as the inferior frontal gyrus) have also been found to be engaged during self-referential processing (for a review see Northoff et al., 2006 and Qin & Northoff, 2011) and given their typical involvement in tasks with strong demands (e.g. tasks requiring verbal monitoring or inference and involving emotions), it was suggested that lateral frontal engagement is related to higher order processing such as autobiographical memory/self (Northoff et al., 2006). Thus, the interaction between self and memory might be implemented in the brain by the interplay between ventral MPFC and lateral frontal cortex. In

support of this hypothesis, two studies have found that the subsequent memory effect for items encoded in reference to the self was related to brain activation in the MPFC and the lateral frontal cortex (anterior prefrontal cortex and superior frontal gyrus) at encoding (Macrae et al., 2004; Leshikar and Duarte, 2012).

Little is known about the brain correlates of the subsequent memory benefit for self-related items (beyond the encoding phase). Different methodologies may serve to examine this question. First, one can examine brain regions engaged during the retrieval of items encoded in reference to the self. To our knowledge, this has been done in only one study. The authors found that retrieval of items that had been encoded in reference to the self was related to brain activation in the posterior cingulate cortex (PCC) in healthy young adults (Leshikar & Duarte, 2012). The PCC has been found to play a role in both episodic retrieval (Genon, Collette, Feyers et al., 2013) and self-related processes (D'Argembeau et al., 2008; for a review see Andrews-Hanna, 2012). Therefore, the PCC could potentially play a role in the retrieval of self-related information in episodic memory. Second, the brain correlates of the subsequent memory benefit for self-related items might be explored by performing correlation analysis between the amplitude of the self-reference effect and variations in local brain functional activity or in local grey matter density. This analysis can only be achieved in populations in which there are large inter-subjects variations, both in the amplitude of the SRE and in brain activity and/or grey matter density. This approach would be particularly appropriate for neurodegenerative disease.

The present study had two main objectives, which led us to design two tasks. Both tasks included two encoding conditions: one engaging self-referential processing and the other engaging other-referential processing. The first aim of this study was to explore the brain



regions related to encoding and retrieval of items in reference to the self and to quantitative retrieval performance for these traits, that is, the SRE, in AD patients. To this aim, a “self-recognition task” was administered during a functional Magnetic Resonance Imaging (fMRI) acquisition. In this task, the SRE effect was assessed by administering a yes/no recognition task. The discrepancy between retrieval performance for items that have been processed with self-reference and retrieval performance for items that have been processed with other-reference provided an estimation of the SRE, that is, memory advantage for self-related items, in each participant (cf. Philippi et al., 2012). This estimation of SRE was subsequently correlated with brain regional grey matter density and functional activity. The second aim of this study was to finely examine the quality of the retrieval of information that has been associated to the self in AD patients, that is, the SRRE, including the amount of details related to the trace. To this aim, a “self-recollection task” was administered to the participants. In this task, the SRRE was assessed by a modified Remember/Know recognition procedure in which patients provided detailed verbal reports on the experienced retrieval process. The latter procedure had two potential advantages. First, it could improve the accuracy of the rating of Remember and Know responses in patients with severe memory impairment. Second, it allows examining the qualitative profile of memory retrieval in the participants. Since both tasks were administered to the same samples of participants, two different sets of adjectives were used for the two tasks.

Since the SRE might depend on the organization and elaboration of the memory trace promoting recollection-based retrieval (i.e. episodic retrieval) for self-related information and since episodic memory is impaired in AD patients, we expected (1) the SRE and SRRE to be impaired in AD patients and (2) the retrieval profile of self-related information in healthy participants to be characterized by qualitative properties of recollection-related processes,

such as richness of associated details or source memory, to a greater extent than in AD patients. Furthermore, at the brain functional level, we expected that the retrieval of information encoded in reference to the self would be related to altered brain activation in the episodic memory network. In particular, the PCC and the hippocampus show early perturbations in AD patients (Salmon et al., 2008; Salmon et al., 2009) and are related to episodic memory deficits in these patients (Genon, Collette, Moulin et al., 2013; Irish et al., in press). Finally, according to Northoff's model, we expected that decreases in SRE would be related to functional and/or structural alterations in the MPFC and/or the lateral frontal cortex.

## II. Methods

### *2.1. Participants*

This study included 21 healthy older control adults (HC) and 21 patients diagnosed with probable AD at a mild stage according to the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's disease and Related Disorders Association (NINCDS-ADRDA) criteria (McKhann et al., 1984). Patients were recruited in the Memory Clinic of the University Hospital of Liège (Belgium). The diagnosis was based on a clinical interview with the patient and a caregiver, and on neurological and neuropsychological examinations. Patients had FDG-PET as a biomarker, and probable AD diagnosis was consistent with new NINCDS-ADRDA's criteria (McKhann et al., 2011). HC were recruited from seniors' organisations in Liège and were paid 15€ for their participation. Ethical approval was obtained from the ethics committee of the University Hospital of Liège and each participant (and a close relative for probable AD patients) gave informed consent to

participate to the study in line with the Declaration of Helsinki. Twelve patients received an acetylcholinesterase inhibitor, 5 patients took ginkgo biloba and 4 patients had no drug treatment for the AD symptoms.

The main demographic and clinical data of the participants are summarized in Table 1. Gender was similarly distributed amongst probable AD and HC groups ( $\chi^2 = .38$ ;  $p = .54$ ). Groups were similar with regard to age [ $t(40) = .08$ ;  $p = .93$ ] and years spent in formal education [ $t(40) = .05$ ;  $p = .96$ ]. Depressive symptoms were assessed in all participants with the 15-item Geriatric Depression Scale (GDS; Yesavage et al., 1983). The GDS scores were similar in probable AD patients and in HC group [ $t(40) = .19$ ;  $p = .85$ ]. Participants were assessed with the Mattis dementia rating scale (Mattis, 1973) and performance was significantly lower in probable AD patients than in HC [ $t(35) = -6.53$ ;  $p < .000001$ ]. In addition, AD patients were assessed with the Mini-Mental State Examination (MMSE, Folstein et al., 1975) for clinical purposes, and mild dementia was an inclusion criterion. Three AD patients and one HC participant did not take part to the second experimental part (i.e. the self-recollection task).

[Table 1 about here]

## **2.2. Materials**

The most frequent 350 words were extracted from Dumas et al.'s (2002) list of person-descriptive words and translated into French. Two adjectives were used as examples during the instructions, 24 adjectives were used in the first practice trials of the self-recognition and self-recollection tasks, and 12 adjectives served in the second practice trials of the self-recognition task. The Self-recognition task comprises 216 adjectives and the Self-recollection task 96 adjectives. The tasks were presented using the Cogent software running on MATLAB

6.1. (Mathworks Inc., Sherborn, MA). The stimuli of the self-recognition and self-recollection tasks were comparable in terms of words length [respectively 8.14 (2.40) and 8.33 (2.21);  $t(310) = -.69$ ;  $p = .49$ ], likability [respectively 3.48 (1.39) and 3.51 (1.38);  $t(310) = -.16$ ;  $p = .88$ ], familiarity [respectively 5.64 (.36) and 5.57 (.46);  $t(310) = 1.34$ ;  $p = .18$ ] and frequency [respectively 31.85 (93.35) and 18.84 (26.48);  $t(310) = 1.33$ ;  $p = .18$ ] according to Kucera and Francis norms (Kucera & Francis, 1967).

### **2.3. Experimental tasks**

For both tasks, in the encoding phase, each adjective was shown for 5 sec to the participants in the middle of a computer screen. The adjectives were always presented in the lexical form that coincided with the gender of the participant. In the self-condition, the participants had to indicate for each trait whether or not it described the self. In the other-condition, the participants had to indicate for each trait whether or not it described King Albert II (for male participants) or Queen Fabiola (for female participants). King Albert II and Queen Fabiola were selected for the other condition since they are famous persons in Belgium and were in the same category of age as the participants (King Albert II was 77 years old at the time of the study and Queen Fabiola was 83 years old). The procedure consisted in a series of study-test runs (9 for the self-recognition task and 4 for the self-recollection task). For each run, 6 adjectives were presented in each condition (self and other, some runs began with the self condition whereas other runs began with the other condition, in such a way that self and other conditions were counterbalanced in the runs). The participants pressed yes/no keyboard buttons with (respectively) the index finger/middle finger to indicate their response. The encoding phase was followed by a recognition phase after an interval of 10 seconds. Although participants knew that the encoding phase would be followed by a recognition phase, they were asked not to voluntarily spend time memorizing the adjectives, but rather to focus on the

requested judgments. In the recognition phase, the 12 adjectives seen in the encoding phase were intermixed with 12 new adjectives. The adjectives were presented in the middle of the screen. For each adjective, the participants had to indicate whether or not they had seen the adjective in the encoding phase. There were 2 counterbalanced lists such that each adjective served as an old and a new item across participants. The recognition phase was followed by a rest of 5 seconds. A short instruction screen was presented before each condition (Self-relevance, Other-relevance and Recognition) for 5 seconds and the question asked to the participants was displayed above the adjective, on the top of the screen, for each condition (respectively “Are-you...?”, “Is Albert-II/Fabiola...?” and “Have you seen...?”). The procedure for the encoding and recognition sessions is illustrated in Figure 1.

[Figure 1 about here]

### 2.3.1. *Self-recognition task*

The self-recognition task was administrated in a 3-T Magnetic Resonance Imaging scanner (scanner description is given below) while acquiring T2\*-weighted functional images at the Cyclotron Research Centre, University of Liège, Belgium. The participants performed 9 runs consisting in one block of Self-relevance and one block of Other-relevance followed by a recognition phase. In the recognition phases, the participant had to indicate for each adjective (within an interval of 8 seconds) whether they had seen it or not in the encoding phase by pressing a yes/no button.

Recognition accuracy for the items encoded in reference to the Self (Self\_accuracy) were computed as the rate of hits for items that have been processed in self-reference minus the rate of false alarms for new items. Similarly, recognition performance for items encoded in

reference to Other (Other\_accuracy) were computed as the rate of hits for items that have been processed in reference to other minus the rate of false alarm on new items.

Furthermore, in order to obtain an estimation of the SRE in each participant, the difference between Self-accuracy and Other\_accuracy was calculated for each participant based on the method used by Philippi et al. (2012). One may reasonably consider that the higher the difference, the greater the advantage of self compared to other on memory performance. Values close to zero are supposed to reflect no advantage of self compared to other on memory performance (Philippi et al., 2012).

### *2.3.2. Self-recollection task*

This task was administered one to four week(s) after the self-recognition task, at the participant's home. As stated above, this task used a different set of adjectives than the set used in the self-recognition task. The participants performed 4 runs consisting in one block of self-relevance encoding and one block of other-relevance encoding followed by a recognition phase. To assess the states of consciousness associated with the retrieval of the items, we used a procedure derived from the traditional Remember/Know procedure (Tulving, 1985; Gardiner, 1988). In traditional Remember/Know procedure, participants are asked to classify as "Remember" items that they recognize through recollection of some episodic details of the encoding context and to indicate "Know" if they have a feeling of familiarity without any contextual information. Some authors reported inadequate understanding of the distinction between the two types of responses in patients with severe episodic memory impairment (Baddeley et al., 2001; Bastin et al., 2004). Other authors have demonstrated the influence of the instructions and the terminology on the accuracy of the participant's answer (McCabe & Geraci, 2009) and have argued that asking participants to provide a verbal report on a recognition test is a better method for assessing states of consciousness associated with

memory retrieval than traditional R/K procedure (McCabe et al., 2011). Therefore, we adapted the procedure by training an experimenter to accurately classify participants' subjective report into the R/K categories. Second, since we were interested in the quality of the recollective experience as assessed by the details remembered from the encoding context, the content of retrieval was further probed by an adapted version of Johnson et al.'s (1988) Memory Characteristic Questionnaire (MCQ). However, since the MCQ is designed to assess autobiographical events, we selected the most relevant criteria for an episodic experimental task. Thus, in this task, when the participants indicated that they had seen an adjective previously, they were asked to describe (without a time limit) the cognitive experience that had driven their answer. Concretely, for each item that the participants indicated having seen previously, the experimenter asked whether they could remember 1) the encoding condition in which they had seen it (that is, the source of encoding, self-relevance versus other-relevance, *condition*), 2) the answer they had given when they had seen the item in the encoding session (*answer*), 3) a thought or a mental image that they had experienced when they had seen the item in the encoding session (*thought*), 4) an emotion that they had experienced when they had seen the item in the encoding session (*emotion*), 5) an episode/a memory of their life that they had retrieved when they had seen the item in the encoding session (*memory*), 6) the temporal position of the item in the encoding session (*temporal context*), or 7) any other detail related to the presentation of the given item in the encoding session such as a sound that attracted their attention when the item has been presented (*other*). If the participant was able to give at least one detail from the encoding context (either during spontaneous verbal report or during the adapted MCQ), the experimenter rated the answer as "Remember". If the participant reported a feeling of knowing the item without being able to provide any detail from the encoding context, the experimenter rated the answer as "Know". Finally, if the participant reported answering by chance, the experimenter rated the answer as "Guess". The

percentages of Remember, Know and Guess responses were corrected for corresponding false alarm rates, i.e. respectively the percentages of Remember, Know and Guess responses given to new items. The Remember and Know responses were first combined to examine global accuracy for items that have been encoded in reference to the self and items that have been encoded in reference to other and therefore to examine whether it replicated the profile of global accuracy found with the self-recognition task. Then, the percentages of Remember and Know responses were analysed separately to examine the effect of self-reference on these responses. According to independence models of recollection and familiarity (Yonelinas & Jacoby, 1995), probabilities for correct Know judgments and false alarms with Know responses were estimated respectively using the following formulae:  $pc(\text{Hits-Know}) = p(\text{Hits-Know}) / (1 - p(\text{Hits-Remember}))$  and  $pc(\text{False alarms-Know}) = p(\text{False alarms-Know}) / (1 - p(\text{False alarms-Remember}))$ . Then  $pc(\text{Hits-Know})$  were corrected for  $pc(\text{False alarms-Know})$ :  $F = pc(\text{Hits-Know}) - pc(\text{False alarms-Know})$ . Thus, F scores refer to familiarity estimates under the assumption of independence.

In the qualitative analysis of the remembered details for old items, the reported responses for “condition” and “answer” were compared to the actual condition and answer given by the participant in the encoding session. Only the responses that accurately reflect the encoding session were taken into account. Inaccurately remembered “condition” and “answer” details for old items were computed as, respectively, “false remembered condition” and “false remembered answer”. All type of details (correct and false) provided by the participants were expressed as percentages of the total number of Remember responses on old items.

#### ***2.4. Images acquisition***

Functional data were acquired on a 3 Tesla scanner (Siemens, Allegra, Erlangen, Germany) using a T2\* sensitive gradient echo EPI sequence (TR = 2040 ms, TE = 30 ms, FA = 90°,



FoV = 220x220 mm<sup>2</sup>, matrix size = 64x64, voxel size = 3x3x3 mm<sup>3</sup>). Thirty-four 3-mm thick transverse slices were acquired, with an interslice gap of 25%, covering the whole brain. The first three volumes were discarded to allow for magnetization equilibrium. A gradient-recalled sequence was applied directly after the functional acquisition to acquire two complex images with different echo times (TE = 4.92 and 7.38 ms respectively) and generate field maps for distortion correction of the echo-planar images (EPI). A structural MR scan was obtained at the end for each participant (T1-weighted 3D MP-RAGE sequence, TR = 1960 ms, TE = 4.4 ms, FoV = 230 x 173 mm<sup>2</sup>, matrix size 384x512x176, voxel size 0.45x0.45x0.9 mm<sup>3</sup>).

Head movement was minimised by restraining the subject's head using a vacuum cushion. Stimuli were displayed on a screen positioned at the rear of the scanner, which the subject could comfortably see through a mirror mounted on the standard head coil.

## 2.5. Images analyses

### 2.5.1. Pre-processing

Preprocessing and analysis of imaging data were performed using SPM8 (Wellcome Department of Imaging Neuroscience, <http://www.fil.ion.ucl.ac.uk/spm>) implemented in MATLAB 6.1. (Mathworks Inc., Sherborn, MA). For each subject, EPI time series were corrected for motion and distortion using Realign and Unwarp (Andersson et al., 2001) together with the FieldMap toolbox (Hutton et al., 2002) in SPM8. Functional scans were realigned using rigid body transformations, iteratively optimised to minimise the residual sum of squares between the first and each subsequent image separately and a mean realigned functional image was then calculated by averaging all the realigned functional scans. This mean functional image was coregistered to the structural T1-image using a rigid body transformation optimised to maximise the normalised mutual information between the two images. Resulted coregistration parameters were then applied to the realigned functional

images. The mapping from subject to MNI space was estimated from the structural image using the ‘unified segmentation’ approach (Ashburner and Friston, 2005). The warping parameters were then separately applied to the functional and structural images to produce normalised images of resolution  $2 \times 2 \times 2 \text{ mm}^3$  and  $1 \times 1 \times 1 \text{ mm}^3$  respectively. Finally, the warped functional images were spatially smoothed using a Gaussian kernel of 8 mm full-width at half maximum (FWHM).

### 2.5.2. Functional analysis

For each participant, BOLD signal were modelled at each voxel, using a general linear model. Nine regressors were defined to cover the two tasks (encoding and recognition). That is, for the encoding task, we distinguished the two encoding conditions (self\_relevance vs other\_relevance) whereas for recognition trials, we distinguished the item status and the types of responses (self\_hits, self\_miss, other\_hits, other\_miss, new\_correct rejection and new false\_alarm) and non-responses. The design matrix also included the realignment parameters to account for any residual movement-related effect. Regressors were convolved with the canonical HRF. A high-pass filter at a cut-off period of 128 sec was used in order to remove the low-frequency drifts from the time series. Serial autocorrelations were estimated with a restricted maximum likelihood algorithm with an autoregressive model of order 1 (plus white noise).

Two main linear contrasts were performed: one to examine brain activity associated to judgments of adjectives in reference to the self by subtracting brain activity related to other\_relevance trials from brain activity related to self\_relevance trials (self\_relevance compared to other\_relevance) and the other to examine brain activity associated to correct retrieval of adjectives that have been processed in reference to the self by subtracting brain

activity related to other\_hits from brain activity related to self\_hits (self\_hits compared to other\_hits).

First-level analyses of individual participants' data were conducted using a fixed-effect approach. The corresponding contrast images were smoothed (6-mm FWHM Gaussian kernel) in order to reduce the remaining noise due to inter-subject differences in anatomical variability. The resulting contrast images were then entered in a second-level analysis, corresponding to a random-effect model. Direct comparisons between the HC and AD groups were performed to examine brain activations that differ in the two groups. A conjunction analysis between the two groups was also performed to reveal brain regions activated by both the patients and the control participants.

In order to examine whether activity changes in VMPFC during self-relevance judgements of items were related to subsequent memory advantage for these items (i.e. SRE), we defined a volume of interest in the VMPFC by drawing a 8 mm radius sphere around the peak of activation in our task (MNI coordinates: -12 42 -4). Then, t values extracted from the contrast image (self\_relevance vs. other\_relevance) in VMPFC were tested for correlation with an estimation of SRE in each participant.

### *2.5.3. Structural analysis*

For each participant, the structural MRI image was segmented using the Voxel Based Morphometry (VBM8) toolbox (Structural Brain Mapping Group, Christian Gaser, Department of Psychiatry, University of Jena, Germany) and normalised to the MNI stereotactic space. The obtained grey matter density images were smoothed (8 mm FWHM Gaussian kernel) and introduced into a simple regression design in SPM8 in order to examine the correlation between regional grey matter density and SRE. Total intracranial volume of

each participant was introduced as a confounding variable in the design matrix in order to account for heterogeneity in global brain volume.

#### 2.5.4. Statistical threshold

The statistical threshold was set at  $P < .05$  FWE-corrected for multiple comparisons or  $P < .001$  uncorrected for multiple comparisons with a-priori hypotheses (self-related and recollection-related brain regions, see introduction).

### III. Results

#### **3.1. Behavioural results**

##### *3.1.1 Self-recognition task*

*Global accuracy.* The mean percentages of Self\_accuracy (hits minus false alarms), Other\_accuracy (hits minus false alarms) and correct rejections for new items (New\_CR) in each group are shown in Table 2. A 2 (Group) by 2 (Condition: Self vs. Other) mixed analysis of variance (ANOVA) on Self\_accuracy and Other\_accuracy as repeated measures revealed a main effect of group [ $F(1,40) = 47.01$ ;  $p < .000001$ ;  $\eta_p^2 = .54$ ], a main effect of the encoding condition [ $F(1,40) = 27.17$ ;  $p < .00001$ ;  $\eta_p^2 = .40$ ] and a significant group by condition interaction [ $F(1,40) = 10.88$ ;  $p < .01$ ;  $\eta_p^2 = .21$ ]. These results are illustrated in Figure 2. A post-hoc analysis (Tukey's test) revealed that the percentages of Self\_accuracy and Other\_accuracy were significantly lower in the AD group than in the HC group (both  $p < .001$ ). In addition, whereas in the HC group the percentage of Self\_accuracy was significantly higher than the percentage of Other\_accuracy ( $p < .001$ ), indicating a SRE, in the

AD group, the percentages of Self\_accuracy and Other\_accuracy were similar ( $p = .54$ ), indicating an absence of SRE.

[Table 2 and Figure 2 about here]

*Individual profiles.* Estimation of SRE by the difference between Self\_accuracy and Other\_accuracy in each participant revealed that whereas 81% of the HC participants had more hits for the items that had been processed in reference to the self (discrepancy between self\_accuracy and other\_accuracy ranging from 5 to 19), only 43% of the AD patients showed this profile of memory advantage for self-related items (discrepancy between self\_accuracy and other\_accuracy ranging from 2 to 15). Thus, in other words, 81% of the HC participants showed a SRE, compared to only 43% of the AD patients. Noteworthy, correlation analyses revealed that this inter-individual variability in SRE was not related to variability in general cognitive/dementia level (as reflected by scores at the Mattis Dementia Rating Scale) neither in AD patients ( $r = .12$ ;  $p = .64$ ) nor in HC ( $r = -.06$ ;  $p = .80$ ).

### 3.1.2. Self-recollection task

*Global Accuracy (computation of the percentages of Remember plus Know responses minus false alarms).* The mean percentages of Self\_accuracy, Other\_accuracy and correct rejections for new items (New\_CR) in each group are detailed in Table 3. A 2 (Group) by 2 (Condition: Self vs. Other) mixed analysis of variance (ANOVA) on Self\_accuracy and Other\_accuracy as repeated measures revealed a main effect of group [ $F(1,36) = 38.75$ ;  $p < .000001$ ;  $\eta_p^2 = .52$ ], a main effect of the encoding condition [ $F(1,36) = 21.18$ ;  $p < .0001$ ;  $\eta_p^2 = .37$ ] and a significant group by condition interaction [ $F(1,36) = 8.58$ ;  $p < .01$ ;  $\eta_p^2 = .19$ ]. A post-hoc analysis (Tukey's test) revealed that the percentage of Self\_accuracy and the percentage of

Other\_accuracy were significantly lower in the AD group than in the HC group (both  $p < .001$ ). In addition, whereas the HC group had greater Self\_accuracy was significantly higher than Other\_accuracy ( $p < .001$ ), in the AD group, the percentages of Self\_accuracy and Other\_accuracy were similar ( $p = .66$ ). Thus, at the quantitative level (accuracy), the results of the self-recollection task replicated the results obtained with the self-recognition task, namely, HC participants showed a SRE at the group level, but AD patients did not.

[Table 3 about here]

*Remember-Know responses.* The percentages of Guess responses (calculated as hits minus false alarms) were very low (range of corrected percentages:  $-6.25 - 4.17\%$  in the whole sample of participants) and, therefore, the analyses were not performed on these responses. The mean percentages of Remember responses for items that have been encoded in reference to the self (Self\_R) and in reference to other (Other\_R) in each group are detailed in Figure 3. A 2 (Group) by 2 (Condition: Self vs. Other) mixed analysis of variance (ANOVA) on corrected Remember responses (hits – false alarms) as repeated measures revealed a main effect of group [ $F(1,36) = 36.63$ ;  $p < .00001$ ;  $\eta_p^2 = .50$ ], a main effect of the encoding condition [ $F(1,36) = 21.78$ ;  $p < .0001$ ;  $\eta_p^2 = .38$ ] and a significant interaction [ $F(1,36) = 15.28$ ;  $p < .001$ ;  $\eta_p^2 = .30$ ]. A post-hoc analysis (Tukey's test) revealed that the percentages of Self\_R and Other\_R were significantly lower in the AD group than in the HC group (both  $p < .001$ ). In addition, whereas the HC group had more Self\_R than Other\_R responses ( $p < .001$ ), indicating a SRRE, in the AD group, the percentages of Self\_R and Other\_R were similar ( $p = .95$ ), indicating an absence of SRRE. Estimates of familiarity (F) for the items encoded in reference to the Self and in reference to Other in each group are illustrated in Figure 3. A 2 (Group) by 2 (Condition: Self vs. Other) mixed analysis of variance (ANOVA)

on estimates of familiarity revealed no main effect of group [ $F(1,36) = .02$ ;  $p < .88$ .  $\eta_p^2 = .00$ ], no main effect of the encoding condition [ $F(1,36) = .99$ ;  $p = .33$ .  $\eta_p^2 = .03$ ] and no interaction [ $F(1,36) = .61$ ;  $p = .44$ .  $\eta_p^2 = .02$ ]. Thus, these results confirmed that, in healthy participants, self-reference at encoding had a subsequent effect only on recollection-based retrieval and not on familiarity-based retrieval. In contrast, in AD patients, self-reference had no effect, neither on recollection-based performance nor on familiarity-based retrieval.

[Figure 3 about here]

*Remembered details.* The percentages of remembered “emotion”, “memory”, “temporal context” and “other” details provided by the participants were very low (means ranging from 0 to 3 percents in both groups), therefore no statistical analysis was performed on these responses. The mean percentages of remembered condition, answer and thought details (expressed as percentages of the total number of Remember responses on old items) in each group are illustrated in Figure 4. A 2 (Group) by 2 (Condition) by 3 (Type of details) ANOVA on the percentages of remembered condition, answer and thought revealed a main effect of group [ $F(1,34) = 38.64$ ;  $p < .000001$ ;  $\eta_p^2 = .53$ ], a main effect of condition [ $F(1,34) = 17.46$ ;  $p < .00001$ ;  $\eta_p^2 = .34$ ], a main effect of type of details [ $F(2,68) = 34.33$ ;  $p < .000001$ ;  $\eta_p^2 = .50$ ] and a significant group by condition interaction [ $F(1,34) = 5.53$ ;  $p < .05$ ;  $\eta_p^2 = .14$ ]. Other interactions were not significant. A post-hoc analysis (Tukey’s test) revealed that in the HC group, the percentages of remembered condition, answer and thought for the items that had been encoded in reference to the self were significantly higher than respectively, the percentages of remembered condition, answer and thought for the items that had been encoded in reference to other (all  $ps < .001$ ), indicating an effect of self-reference on

contextual retrieval. In contrast, in the AD group, there was no between-condition difference on the percentages of remembered condition, answer and thought, indicating no effect of self-reference on contextual retrieval.

[Figure 4 about here]

A 2 (Group) by 2 (Condition) by 2 (Type of details) ANOVA on the percentages of false remembered condition and false remembered answer for the items that had been encoded respectively in reference to the self and in reference to other as repeated measures revealed a main effect of group [ $F(1,34) = 32.31$ ;  $p < .00001$ ;  $\eta_p^2 = .49$ ], a main effect of type of details [ $F(1,34) = 82.42$ ;  $p < .000001$ ;  $\eta_p^2 = .71$ ] and a significant group by type of details interaction [ $F(1,34) = 35.82$ ;  $p < .00001$ ;  $\eta_p^2 = .51$ ]. Other interactions were not significant. A post-hoc analysis (Tukey's test) revealed that the percentages of false remembered condition were significantly higher in the AD group than in the HC group for both encoded in reference to the self and the items encoded in reference to other (both  $ps < .001$ ). In contrast, the percentages of false remembered answer were similar in both groups. Congruently, the post-hoc analysis also revealed that the percentages of false remembered condition was significantly higher than the percentages of false remembered answer (across both conditions) in the AD group (both  $ps < .001$ ), while there was no difference in the HC group.

To summarize, our behavioural data revealed that, at the group level, self-reference had an effect on global accuracy (SRE), on recollective experience (SRRE) and on contextual retrieval (including source memory) in HC participants, but not in AD patients. Therefore, at the brain level, we examined functional imaging data to investigate brain regions directly



engaged during self-referential encoding and during correct retrieval of items encoded in reference to the self.

### **3.2. Functional Imaging Results**

#### *3.2.1. Encoding: self-referential processing*

No region was found to be significantly more activated in HC than in AD and vice versa during judgment of self-relevance compared to judgment of other-relevance (self-relevance versus other-relevance) at the selected threshold ( $p_{\text{corrected}} < .05$  or  $p_{\text{uncorrected}} < .001$ ) when performing direct statistical comparisons (HC > AD and AD > HC).

A conjunction analysis in the HC and AD groups revealed that both groups activated the ventromedial prefrontal cortex (VMPFC; cluster size = 80, Z-value = 3.80,  $p_{\text{uncorrected}}$  value = .001, MNI coordinates = -12 42 -4) during judgment of self-relevance compared to judgement of other-relevance (self-relevance versus other-relevance). This result is illustrated in Figure 5.

[Figure 5 about here]

#### *3.2.2. Correlation analysis*

The correlation between brain functional changes in VMPFC (coordinates: -12 42 -4, sphere's radius: 8mm) related to self-relevance judgements and estimation of SRE (difference between Self\_accuracy and Other\_accuracy) was not significant, neither in the HC group nor in the AD group.

### 3.2.3. *Recognition: retrieval of self-related items*

No region was found to be significantly more activated in HC than in AD and vice versa during correct recognition of an item that has been processed in reference to the self (self\_hits) when compared to correct recognition of an item that has been processed in reference to other (other\_hits) at the selected threshold when performing direct statistical comparisons (HC > AD and AD > HC). Similarly, a conjunction analysis in the HC and AD yielded no significant result at the selected threshold. It is noteworthy that this lack of significance was observed despite the fact that the number of events in each condition (self\_hits and other\_hits) and each participant was sufficient (minimum 18) to perform statistical contrast.

To summarize, the analysis of brain functional data revealed that during self-reference encoding, both AD and HC participants activated a self-related brain region, the VMPFC. However, functional activity in this region during encoding was not related to subsequent memory advantage, that is, SRE. The analyses of brain regions directly engaged during correct retrieval of items encoded in reference to the self failed to reveal any significant results. Next, we performed correlation analyses between SRE and grey matter density.

## 3.3. *Structural Imaging Results*

### 3.2.1. *Group comparison*

In agreement with previous studies, a whole brain statistical group comparison revealed that grey matter density was significantly lower in posterior midline structures (i.e. posterior cingulate/inferior precuneus) and medial temporal lobes (hippocampus and parahippocampal cortices) in AD patients compared to HC (Buckner et al., 2005).

### 3.2.2 Correlation analysis

There was no significant correlation between estimations of SRE (difference between Self-accuracy and Other\_accuracy, i.e. memory advantage for items that have been processed in reference to the self) and grey matter density in HC participants.

In AD patients, estimations of SRE were significantly and positively correlated with grey matter density in the lateral prefrontal cortex (LPFC) and more particularly, in the right middle/superior frontal gyrus (cluster size = 93, Z-value = 4.24,  $p_{\text{uncorrected}}$  value = .001, MNI coordinates = 30 45 4). This result is illustrated in Figure 6.

[Figure 6 about here]

To summarize, as expected, the structure of AD patients' brains is characterized by grey matter atrophy in the posterior midline structures and the medial temporal lobe. Moreover, reduced and variable SRE is related to grey matter density in the lateral prefrontal cortex in these patients.

## IV. Discussion

At the behavioural level, our results revealed that in healthy older participants, memory performance was quantitatively better for self-related items than for other-related items, that is, healthy older participants showed a SRE. In contrast, in our sample of mild AD patients, memory performance was similar for self-related items and other-related items, showing, at the group level, an absence of SRE in AD patients. As expected, in healthy older participants, the retrieval of self-related items was more frequently associated with a recollective

experience (i.e. episodic retrieval) than the retrieval of other-related items, demonstrating a SRRE. In contrast, in the AD patients, the retrieval of self-related items and the retrieval of other-related items were similarly associated with poor recollective experience. Interestingly, familiarity processes for the retrieval of self-related items and other-related items were similarly engaged in both healthy older participants and AD patients, suggesting relatively preserved familiarity in mild AD. Our analysis of the remembered details revealed that in healthy older participants, recollection of information that had been encoded in reference to the self was associated with more details from the encoding phase (mainly the source, that is, the encoding condition and the answer that the participant had given) than recollection of information that had been encoded in reference to the other person. This difference was not observed in AD patients.

Consistently with the hypothesis that the specificity and the relational quality of the information encoded in reference to the self promote recollection-based processes at retrieval in healthy populations, in healthy older participants, the retrieval of self-related information is associated with the recollection of details from the encoding context. Importantly, AD patients experienced poor recollection for both self-related and other-related information. In particular, the retrieval of self-related information in AD patients lacks contextual details. The results are also congruent with previous studies that have revealed that the retrieval of autobiographical memories in AD patients is deprived of contextual details (Irish, Hornberger, et al., 2011; Irish, Lawlor, et al., 2011; Piolino et al., 2003; Martinelli et al., 2013), suggesting that high-order self-related processes are impaired in AD patients.

From a theoretical viewpoint, the current findings suggest that the interaction between self and memory processes may be altered in AD patients. In the framework of the Self-Memory

System (SMS, Conway & Pleydell-Pearce, 2000; Conway et al., 2001), the SRE and SRRE might reflect the fact that self-relevant information is integrated with related knowledge in the autobiographical memory knowledge base, whereas self-unrelated information is not and therefore remains as more fragile representations. Similarly, in the framework proposed by Northoff et al. (2006), the SRE and SRRE would occur because self-referential processing at encoding had activated the core self that further promoted those stimuli to be elaborated in higher-order processing, such as autobiographical memory/self. Therefore, the impaired interaction between self and memory in AD patients might be conceptualized as the altered interaction between the core self and the autobiographical self.

Individual profiles of memory advantage for self-related items revealed that the great majority of healthy participants showed a SRE in their memory performance, whereas most of the AD patients did not. However, some AD patients did show a memory advantage for self-related items. This variability across patients might indicate that despite the frequent impairment of interaction between self and memory in AD patients, it appears to be relatively preserved in some patients. In a systematic review of qualitative and quantitative studies of the self in dementia, Caddell and Clare (2010) have highlighted the divergence of findings in studies that have examined the self in AD patients: some findings suggested that it is relatively preserved and others indicated that it is impaired. This heterogeneity in findings might partially be due to large inter-subjects variability in AD patients' samples. In our study, this variability did not appear to be related to variability in dementia severity in AD patients. The fact that self-related abilities are not systematically disrupted by the AD pathological process, and are thus variable across patients, gave us the opportunity to examine functional and structural brain variations in relation to the SRE (see below).

Our functional neuroimaging results showed that AD patients engaged the VMPFC as HC did during self-referential judgments. This result differs from previous findings indicating that MPFC engagement was not significant in AD patients during self-referential judgments (Ruby et al., 2009; Zamboni et al., 2012). This divergence may be explained by methodological differences. Previous studies compared brain activity during processing of adjectives in reference to the self with brain activity during processing of adjectives in reference to a familiar and somewhat intimate other (close relative, friend or caregiver). In our study, the comparison was made with processing of adjectives in reference to the self with brain activity during processing of adjectives in reference to a non-intimate, famous other (King Albert II or Queen Fabiola). Therefore, one might speculate that while AD patients' neurocognitive system may normally differentiate the self from a personally remote other (King or Queen), it may not as clearly differentiate the self from a close other. This dysfunction may be related to the "permeability of the ego boundaries" that characterizes neuropathologies of the self described by Feinberg (2011). Findings in favour of this speculation can be found in Zamboni et al.'s study where AD patients had greater activation in the MPFC for judgment of close other-relevance than for judgment for self-relevance (direct statistical comparison other > self). This interpretation should be investigated further in future studies by directly comparing brain activations associated with the processing of items in reference to the self, to a close other and to a remote other in AD patients.

Interestingly, the engagement of the VMPFC during self-referential judgments at encoding in AD patients did not induce any memory advantage for subsequent episodic retrieval at the group level. Particularly, the memory advantage for items that have been processed in reference to the self was not related to brain functional changes in the VMPFC during self-referential judgements at encoding neither in AD patients nor in healthy older participants.

According to Northoff et al. (2006), the VMPFC supports the core self, that is, self-referential process per se. The linkage between self-referential stimuli and memory is supported by the autobiographical self, which is related to the lateral prefrontal cortex. Accordingly, at the brain structural level, our results revealed that the amplitude of the memory advantage for self-related items was positively correlated with grey matter density in the right middle/superior frontal gyrus (lateral PFC) in AD patients. Two meta-analyses of fMRI studies (Wicker et al., 2003; Whitfield-Gabrieli et al., 2011) revealed that brain activity in this region is increased during resting state in healthy young participants suggesting that this region may be engaged during internally-oriented processes. Interestingly, this region has also been found to be related to episodic memory retrieval (Lepage et al., 2000; Kim, in press; Skinner and Fernandez, 2007) or recollection-based controlled retrieval (Gallo et al.; 2009). Altogether, these findings suggest that the LPFC (particularly in the right hemisphere) plays a role in self-related processes and high-order (controlled) memory-related processes. Therefore, one may hypothesize that variations in the memory advantage for self-related items is related to variations in high-order abilities that monitor the interaction between self and memory in AD patients, in line with Northoff et al.'s hypothesis.

No significant correlation was found between grey matter density and the amplitude of SRE in HC participants. This does not necessarily mean that the MPFC or LPFC do not play a role in memory advantage for self-related information in these participants. Rather, the absence of results may suggest that variations in grey matter density and/or amplitude of SRE is insufficient in these participants to yield a significant correlation.

Since our behavioural results suggest that the retrieval of information that has been processed in reference to the self is more associated with recollection-related processes than other

information in HC participants but not in AD patients, one might expect brain activation related to self\_hits to be more associated with brain regions supporting episodic memory (and self-related processes such as the PCC) in the HC group than in the AD group. However, statistical group comparisons of brain activity related to correct retrieval of items that have been processed in reference to the self (self\_hits compared to other\_hits) yielded no significant results. In a previous fMRI study of memory retrieval in HC participants and AD patients, we found that despite lower recollection-based performance than HC participants, AD patients activated the PCC as HC participants. Connectivity analyses in this previous study revealed, however, that functional connectivity of the PCC during episodic retrieval was impaired in AD patients (Genon, Collette, Feyers et al., 2013). This suggests that brain functioning supporting recollection-related processes is complex and that impaired recollection function in AD patients might be related to subtle functional changes (probably in terms of connectivity) within a large-scale brain network. Therefore, univariate analyses in line with the assumption of functional segregation and targeting regionally specific effects of particular items in the brain may not be the optimal analysis to examine complex function such as recollection in AD patients. In addition, our current behavioural results suggest that retrieval of other-related information is also associated with recollection-related processes in both groups (although to a smaller extent than self-related information in HC). Therefore, it may be the case that differential functioning in the recollection-related brain network for self\_hits and other\_hits is not sufficient to reach the significance threshold with a univariate analysis.

In summary, our study provides new behavioural and imaging findings on the interaction between self and memory in AD patients. At the behavioural level, whereas the retrieval of self-related information is facilitated and associated with rich recollective experience in



healthy older participants, the retrieval of self-related information in AD patients is, as the retrieval of other kinds of information, low and poorly associated with recollection processes. At the cerebral level, memory performance for retrieving self-related information does not depend on MPFC activation at encoding (during self-referential judgments). Rather, the decreased memory advantage for self-related information in AD is associated with impaired grey matter density in the LPFC, a brain region that may support high-order processes involved in the interaction between self and memory. In conclusion, these findings suggest that even if patients with Alzheimer dementia engage a self-related region when performing self-referential judgment, the retrieval of self-related memories is quantitatively and qualitatively impaired.

More generally, many patients with AD do not fully acknowledge the cognitive and behavioural changes that modify the person they used to be (a condition called anosognosia; for a review, see e.g. Agnew & Morris, 1998; Mograbi et al., 2009). According to Morris & Mograbi (in press), anosognosia in AD may be related to impaired memory processing of self-related information. From this perspective, the current study suggests that, whereas in healthy older people, the connection of newly encountered information to the self promotes subsequent high quality memories, in AD patients this phenomenon is modified leading to poor memory for recently encountered self-related information. Our data also suggest that perturbations in lateral prefrontal regions (in particular in the right hemisphere) might play a role in these modifications. Given that anosognosia in AD patients has been found to be related to abnormalities in lateral prefrontal regions (Reed et al., 1993; Sedaghat et al., 2012) and to impaired autobiographical memory performance (Naylor & Clare, 2008), one might speculate that impaired interaction between self and memory related to perturbations in lateral prefrontal regions might play a role in anosognosia of some AD patients. Future studies could

test this hypothesis by examining the relationship between anosognosia and memory performance for recently self-related encountered information in AD patients.

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Figure 1. Encoding (left) and recognition (right) procedures that served for the self-recognition task and the self-recollection tasks. Screens were separated by a fixation cross not represented here.

Figure 2. Accuracy scores (percentages of hits minus false alarm) for items encoded in reference to the self and in reference to other. Standard errors are represented by errors bars. \*Self compared to Other  $p < .05$ .

Figure 3. Percentages of R (Remember responses minus false alarm) and F (familiarity estimates based on Know responses minus false alarm) for items encoded in reference to the self and in reference to other. Standard errors are represented by errors bars. \*Self compared to Other  $p < .05$ .

Figure 4. Percentages of remembered details for items encoded in reference to the self and in reference to other. Standard errors are represented by errors bars. \*Self compared to Other  $p < .05$ .

Figure 5. Brain region commonly activated by HC and AD group (conjunction analysis) during self-relevance judgements (self-relevance vs other-relevance).  $p < .001$  uncorrected for the whole brain volume.

Figure 6. Positive correlation between grey matter density and estimation of SRE in AD group.  $p < .001$  uncorrected for the whole brain volume.

Table 1. Demographic and clinical data in studied groups.

	HC	AD
<i>n</i> (M/F)	21 (10/11)	21 (12/9)
Age (years)	76.0 (4.9)	76.1 (6.0)
Years of education	10.8 (2.5)	10.8 (3.5)
GDS scores	2.7 (2.4)	2.8 (2.5)
Mattis scores*	139.1 (3.1)	126.6 (7.7)
MMSE		23.6 (2.0)

AD: Alzheimer disease. HC: Healthy controls. GDS: Geriatric Depression Scale. MMSE: Mini Mental State Examination. Values are expressed as mean and (standard deviation) for age, years of education, GDS scores and Mattis scores. M = male; F = female; *n* = size, \**p* < .001.

Table 2. Percentages of correct responses in the AD and HC groups (*self-recognition task*).

	Self_accuracy	Other_accuracy	New_CR
AD	38.4 (18.6)*	35.2 (15.4)*	77.6 (12.6)*
HC	75.6 (11.3)	61.2 (17.4)	89.2 (5.9)

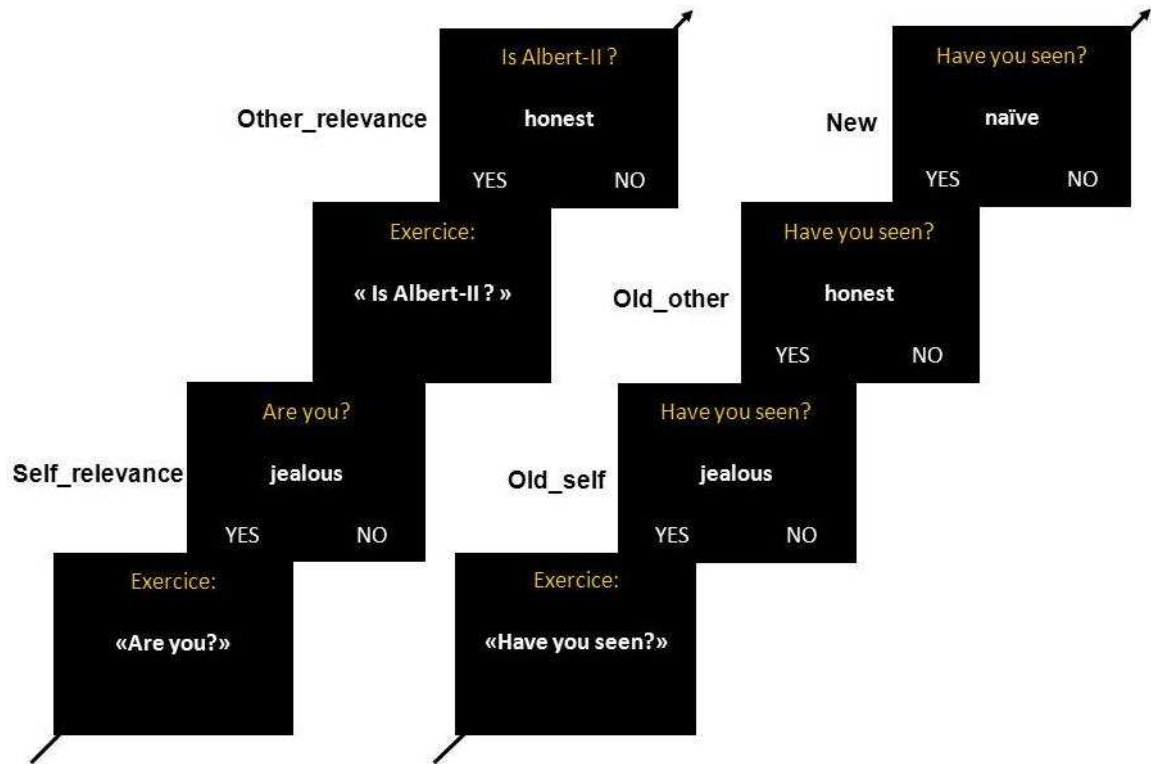
Accuracy scores are expressed as percentage of hits minus percentage of false alarm. CR; correct rejections. Data are presented as means  $\pm$  standard deviation. \*The percentage is significantly lower in the AD group than in the HC group at  $p < .01$ .

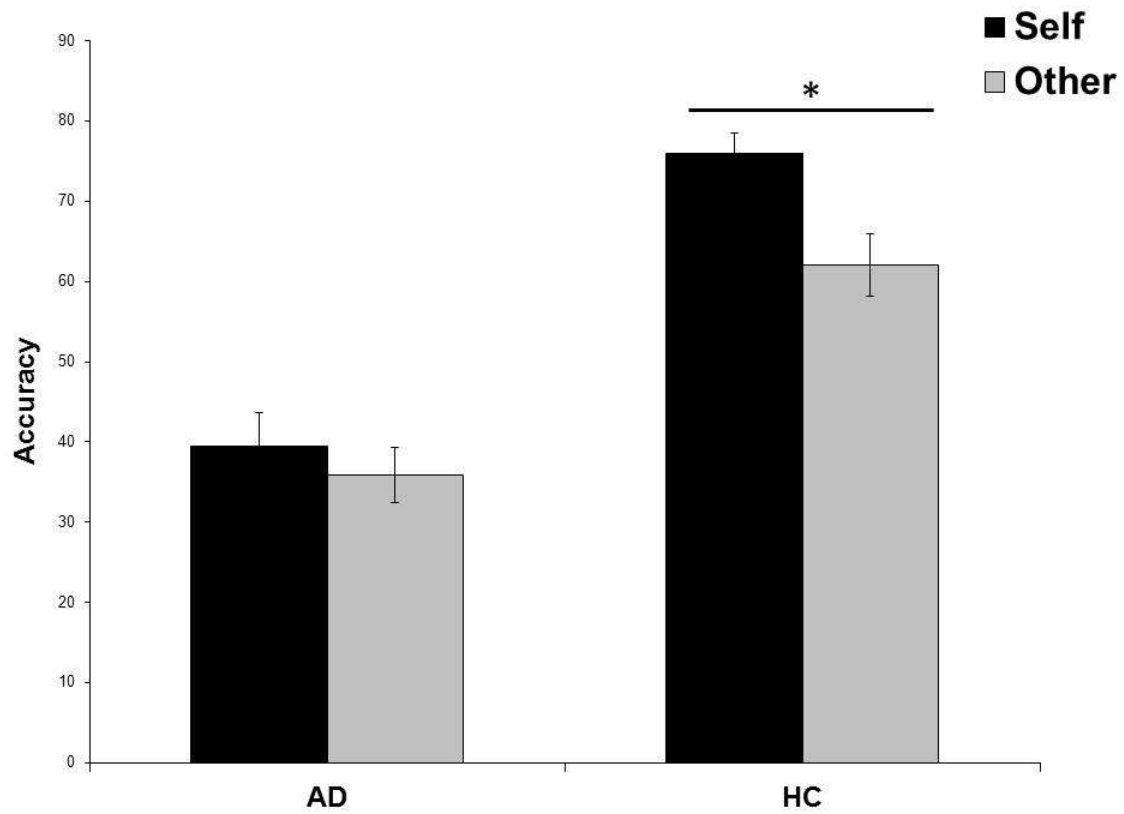


Table 3. Percentages of correct responses in the AD and HC groups (*self-recollection task*).

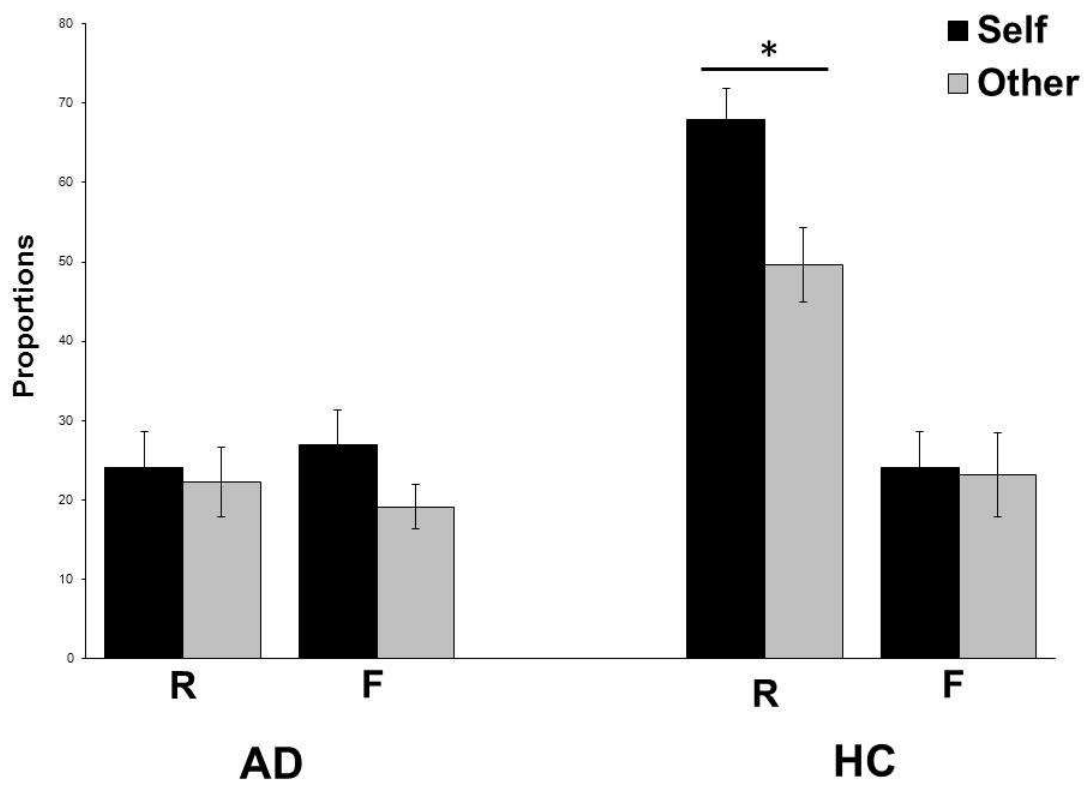
	Self_accuracy	Other_accuracy	New_CR
AD	35.5 (20.8)*	32.1 (14.3)*	78.8 (14.8)*
HC	75.1 (14.0)	59.5 (20.7)	94.5 (6.1)

Accuracy scores are expressed as percentage of hits (computations of Remember and Know responses) minus percentage of false alarm. CR; correct rejections. Data are presented as means  $\pm$  standard deviation. \*The percentage is significantly lower in the AD group than in the HC group at  $p < .01$ .

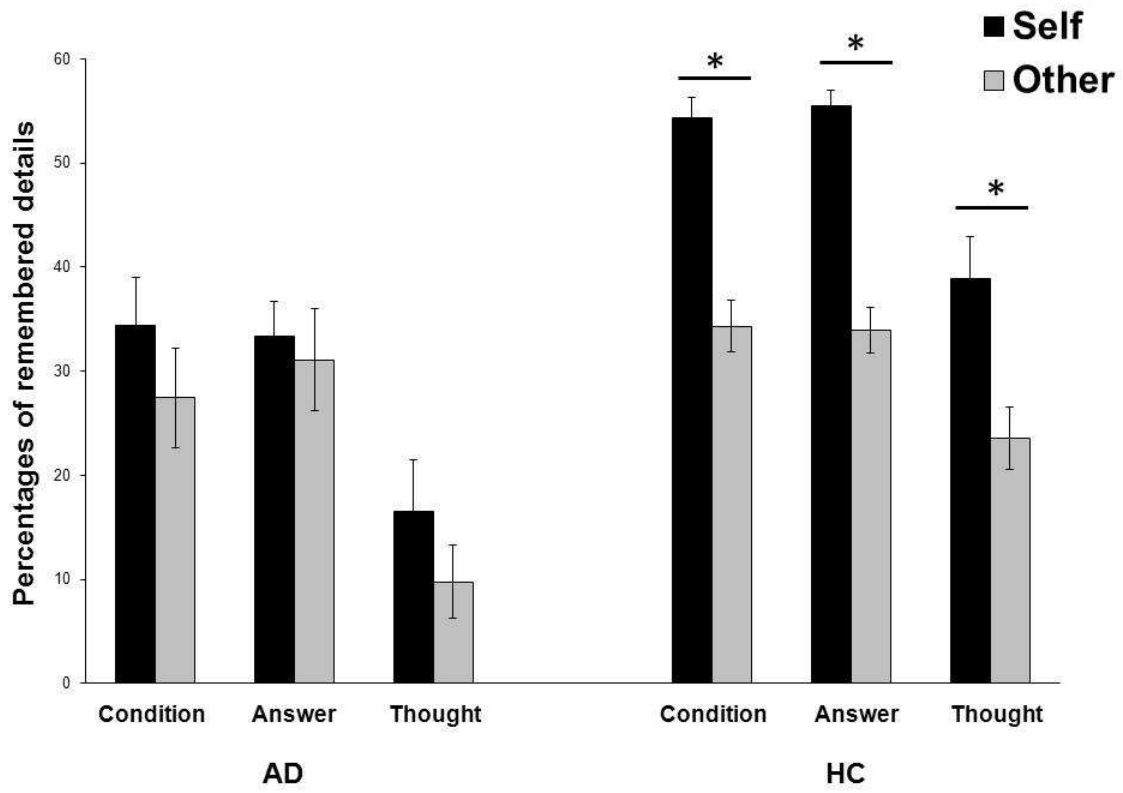


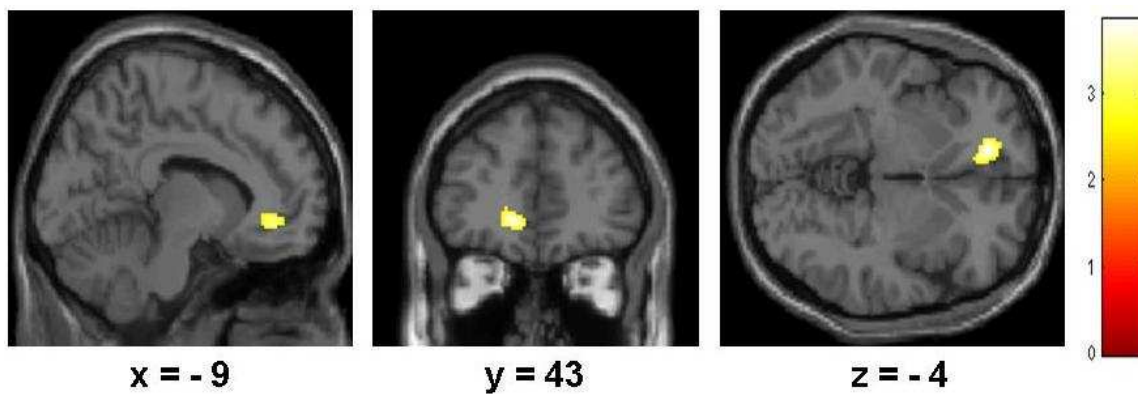


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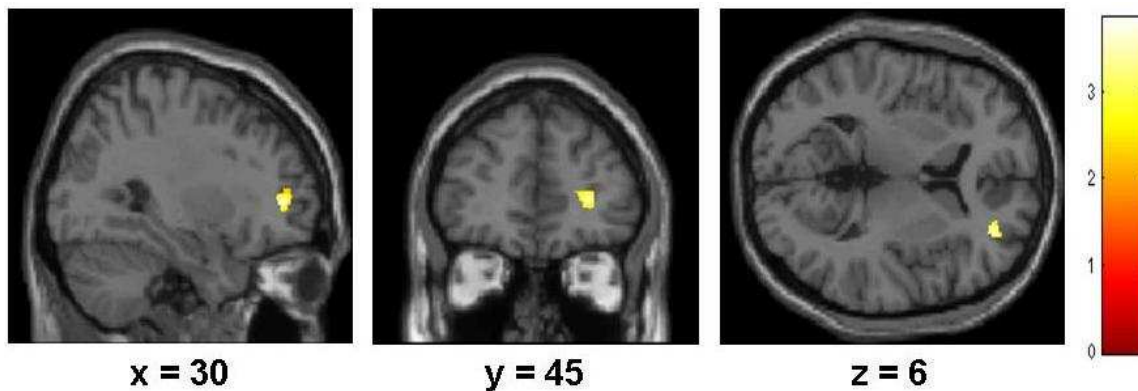


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