Do Alzheimer's disease patients benefit from prior-knowledge in associative recognition memory?

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Abstract

Objective: Although the influence of prior knowledge on associative memory in healthy aging has received great attention, it has never been studied in Alzheimer's disease (AD). This study aimed at assessing whether AD patients could benefit from prior knowledge in associative memory and whether such benefit would be related to the integrity of their semantic memory

Method: Twenty-one AD patients and 21 healthy older adults took part in an associative memory task using semantically related and unrelated word pairs and were also submitted to an evaluation of their semantic memory.

Results: While participants of both groups benefited from semantic relatedness in associative discrimination, related pairs recognition was significantly predicted by semantic memory integrity in healthy older adults only.

Conclusion: We suggest that patients benefitted from semantic knowledge to improve their performance in the associative memory task, but that such performance is not related to semantic knowledge integrity evaluation measures because the two tasks differ in the way semantic information is accessed: in an automatic manner for the associative memory task, with automatic processes thought to be relatively preserved in AD, and in a controlled fashion for the semantic knowledge evaluation, with controlled processes thought to be impaired in AD.

Keywords: Episodic memory; Associative memory; Semantic memory; Prior knowledge; Alzheimer's disease; Aging

Introduction

Semantic memory (general knowledge about the world) is distinguished from episodic memory (memory for personally experienced events) (Tulving, 1972). Although these two systems were shown to be dissociable by a large body of neuropsychological studies, they are thought to interact (Fang, Rüther, Bellebaum, Wiskott, & Cheng, 2018; Greenberg & Verfaellie, 2010). Notably, healthy individuals' episodic memory encoding and retrieval processes are enhanced when the to-be-remembered new information can be integrated within and is consistent with pre-existing knowledge about the world – schemas –which provides an organizational structure to support learning (Bartlett, 1932; Bird, Davies, Ward, & Burgess, 2010; Greve, van Rossum, & Donaldson, 2007; Hemmer & Steyvers, 2009).

Intact semantic knowledge can also support declining episodic memory. For instance, in normal aging, semantic memory either improves or remains stable (Umanath & Marsh, 2014), whereas episodic memory declines, partly due to difficulties in forming and retrieving associations between elements (Naveh-Benjamin, 2000). Critically, the age-related associative memory deficit can be diminished when the to-be-learnt associations are congruent with prior knowledge (semantically related word pairs, Naveh-Benjamin, Hussain, Guez, & Bar-On, 2003; Patterson, Light, Van Ocker, & Olfman, 2009; groceries-price associations, Castel, 2005; age-face associations, McGillivray & Castel, 2010; name-adjective associations, Smyth & Naveh-Benjamin, 2018; objects in relational learning tasks, Ostreicher, Moses, Rosenbaum, & Ryan, 2010; Ryan et al., 2016). When semantic support can be used as a strong cue of past exposure, older individuals perform memory tasks as efficiently as younger individuals. Older adults' overreliance on their prior knowledge could be explained either by the strength of pre-existing knowledge relative to recent episodic memories, or by its greater accessibility in memory (Umanath & Marsh, 2014). Similar results were put forward in medial temporal lobe amnesia. For instance, Kan, Alexander, and Verfaellie (2009) demonstrated that amnestic patients' episodic memory was enhanced when the to-be-remembered information

(objects and prices) could be anchored within pre-existing knowledge, provided that semantic memory was preserved (see also Moses et al., 2009). Conversely, an impairment in semantic knowledge could impair the acquisition of new episodic memories (Fang et al., 2018; Greenberg & Verfaellie, 2010). Such findings thus have implications for rehabilitation strategies for individuals with memory disorders.

A predominant impairment of episodic memory is also observed early in the course of Alzheimer's disease (AD) and includes an alteration of associative memory (Bastin et al., 2014; Gallo, Sullivan, Daffner, Schacter, & Budson, 2004; Sperling et al., 2003; Wolk, Signoff, & DeKosky, 2008). In autobiographical memory, AD is accompanied by a shift from episodic to semantic memories (El Haj, Antoine, Nandrino, & Kapogiannis, 2015), suggesting that semantic memory could compensate for the deteriorated episodic memory. However, to our best knowledge, few studies have investigated whether AD patients could benefit from prior-knowledge in episodic memory (Backman & Herlitz, 1990; Lipinska, Backman, & Herlitz, 1992). These studies showed that AD patients benefitted from prior knowledge in memory only when they were encouraged to generate elaborative statements at encoding, such that it probably increased prior-knowledge activation. Nevertheless, these works assessed item rather than associative memory. No study has investigated whether AD patients could benefit from prior-knowledge to support their markedly impaired associative recognition.

One potential reason for this lack of investigation could be that AD patients actually do demonstrate a progressive deficit in semantic memory (Chertkow, Whatmough, Saumier, & Duong, 2008; Laisney, Desgranges, Eustache, & Giffard, 2010; Rogers, Ivanoiu, Patterson, & Hodges, 2006). Still, semantic memory is not uniformly affected in AD. A central debate concerning semantic memory decline in AD concerns the contribution of semantic memory access difficulties (i.e. semantic retrieval), semantic knowledge deterioration (i.e. semantic content) and/or semantic process dysfunction (i.e. semantic regulation) (Reilly, Peelle, Antonucci, & Grossman, 2011). Some authors

proposed that semantic impairment in early AD is attributed to retrieval difficulties, followed by semantic storage alteration with the evolution of the disease (Cardebat, Aithamon, & Puel, 1995). Those accounts are thus not mutually exclusive in explaining semantic deficits in AD (Rogers & Friedman, 2008). Among semantic knowledge deterioration theories, some researchers proposed that, as AD progresses, semantic memory follows a bottom-up degradation, with subordinate attributes (e.g., functional and perceptual features) declining before superordinate knowledge (e.g., categorical features) (Bottom-up Process Theory; Huff, Corkin, & Growdon, 1986). Furthermore, there is a category effect whereby AD preferentially affects living things compared with manufactured objects (Chertkow et al., 2008), possibly due to the small semantic distance between living concepts (Zannino et al., 2006).

In this context, the present study assessed whether mild AD patients' associative memory could be improved when the to-be-learnt associations could be anchored within preserved prior-knowledge (here, categorical relationship between words), similar to amnesia or healthy aging. We predicted that the benefit from prior-knowledge in associative memory in AD patients would vary as a function of the relative integrity of their semantic memory.

Methods

Participants

Twenty-one participants with a diagnosis of probable mild AD (MMSE>21; range: 22-28; M=24.57; SD=1.75) and 21 control participants took part in the experiment (see Table 1). All participants were native French speakers. AD patients were all at a mild dementia stage and suffered from memory impairments (amnestic subtype). They were recruited from the Memory Clinic (Liège) and voluntarily participated in the study. Clinical AD diagnosis was made according to the guidelines provided by the National Institute on Aging-Alzheimer's Association workgroups (McKhann et al., 2011). No detailed and systematic neuropsychological information regarding AD patients was

available from the Memory Clinic because cognitive assessment varied from one patient to another. Exclusion criteria were additional neurological or psychiatric disorder, systemic disease as well as any medication that could negatively interfere with their cognitive functioning. Healthy older adults were recruited from the Liège area. None of them reported neurological or psychiatric history, nor did they show any sign of cognitive decline, as assessed with the Mattis Dementia Rating Scale, which indicated better performance in older adults compared with AD patients (scores were unavailable for two AD patients). The two groups were matched in terms of age and education. All participants gave a written informed consent and the study was approved by the Ethics Committee of the Faculty of Psychology of the University of Liège.

[Table 1 about here]

Materials

A total of 144 words were selected among the most frequently generated words in response to a category term (free association norms, Dubois & Poitou, 2002). The words belonged to 10 different semantic categories representing either natural (n=5: animals, trees, vegetables, flowers, occupations) or manufactured (n=5: drinks, tools, toys, vehicles, clothes) elements. Thirty related word pairs were created by organising 6 words from each category into 3 pairs (e.g., tomato-cucumber, turnip-celery, leek-spinach). The pairs were selected in order to form categorical associations only, and phonological resemblance between words of a same pair was controlled for by avoiding syllables repetition from one word to the other. Thirty unrelated word pairs were created by combining words from different categories (e.g., willow-rattle, pea-horse, brain-tram). Each word was presented only once during encoding, either in a related or in an unrelated combination. Recombined pairs for the associative memory test were created by switching words across the studied pairs, within a same category for the related pairs or across categories for the unrelated pairs (e.g, tomato-celery for related pairs or mouse-harp for unrelated pairs). The remaining words served as stimuli for the

practice session (24 words) and to test item memory in a separate "item test" (3 new words from a studied category and 3 new unrelated words in each list).

The 30 related and 30 unrelated word pairs were divided in two lists, each comprising 15 related and 15 unrelated word pairs, in such a way that five categories appeared in one list, but not in the other. The two lists were used to create two study-test cycles. The order of presentation of the lists, the status of the pairs as intact or recombined in the memory tests, as well as the order of item and associative memory tests (see Procedure below) were counterbalanced across participants. The order of pair presentation within each list was randomized.

To ensure that the pairs matched with their relatedness condition (semantically related or unrelated), we asked 10 other participants (age: M=28.72, SD=15.04) to rate the relatedness of each pair on a Likert scale from 1 (completely unrelated) to 10 (completely related). The pairs with a mean higher than 7 were classified as related, and those lower than 4 as unrelated pairs.

Procedure

Participants were tested individually. Stimuli were presented on a laptop computer using the E-Prime software. Two study-test cycles were completed with a short break (2 minutes) in-between. For each cycle, the encoding phase comprised 30 word pairs intermixing 15 related and 15 unrelated pairs. Each pair was presented for 6 seconds, with a 1-s inter-stimuli interval composed of a 500ms blank screen followed by a 500ms fixation cross. Study instructions were intentional and the participants knew that their memory would be assessed. During the retention interval, participants had to count backwards during one minute. Two yes-no recognition memory tests followed, one "item test" assessing memory for single items, thought to be better preserved in AD than associative memory, and one "associative test" assessing memory for the associations between items. Responses were self-paced. In the item test, participants viewed 18 words (6 old from related pairs, 6 old from unrelated pairs, 3 new related to a studied category, 3 new unrelated to any studied category). They

had to decide whether each word had been previously presented. In the associative recognition memory test, 24 word pairs were presented: 12 related (6 intact and 6 recombined) and 12 unrelated (6 intact and 6 recombined). For each pair, participants had to indicate whether they had seen the exact same pair at encoding (intact) or not (recombined). Prior to the task, there was a practice session in order to familiarize the participants with the procedure.

We also assessed the integrity of patients' semantic knowledge using the French version of the Semantic Knowledge Questionnaire (SKQ, Simoes Loureiro & Lefebvre, 2015). This questionnaire was initially created by Laiacona, Barbarotto, Trivelli, and Capitani (1993) and assesses semantic memory according to the Bottom-up Process Theory (Huff et al., 1986). The French version of the questionnaire consists of 30 items: 15 items are natural (5 fruits, 5 vegetables, 5 animals) and 15 are manufactured (5 tools, 5 vehicles, 5 furniture). For each item (e.g. helicopter), four forced-choice questions requesting different kinds of semantic information are asked. They respectively evaluate superordinate general knowledge (Q1, "is the helicopter a vegetable, an object or an animal?"), superordinate intracategorical knowledge (Q2, "is the helicopter a vehicle, an utensil or a furniture?"), subordinate perceptual knowledge (Q3, "does the helicopter have a propeller, wings or wheels ?") and subordinate functional features (Q4, "does the helicopter run on wind, electricity or fuel ?"). Participants selected the items in a self-defined order. When an item was selected, the first question appeared on the screen and was read aloud by a female voice. The experimenter pressed the response key corresponding to participants' answer. This procedure was then repeated for the three next questions and for the 29 remaining items. Each error was counted. A global error score was obtained as well as specific error scores for the four question types and for both categories of objects (natural versus manufactured objects).

Statistical analyses

To obtain a measure of participants' global memory performance and response bias, we computed the discrimination index *d'* and criterion C using hits and FA rates (Macmillan & Creelman, 2005). Repeated measures ANOVAs were used to explore differences across groups and conditions and their interaction. We also implemented linear regression analyses in order to investigate the relationship between the measures from the two tasks (the SKQ and the associative memory task) for each group separately. The statistical threshold was set at $p < .05$.

Results

Because the effect of study-test cycle was not of primary interest, we collapsed the two study-tests cycles for the main analyses. The *d'* scores were submitted to a 2 (group: control, AD) x 2 (test: item, associative) x 2 (relatedness: related, unrelated) repeated-measures ANOVA (see Figure 1). This revealed a main effect of group, $F(1,40)=29.80$, $p<.001$, $\eta_p^2=.43$, reflecting better discrimination performance for controls (M=1.35; SD=0.68) compared with patients (M=0.73; SD=0.66), a main effect of test, $F(1,40)=82.35$, $p<.001$, $\eta_p^2=.67$, with higher *d'* in the item (M=1.38; SD=0.64) than in the associative test (M=0.71; SD=0.67) but no test x group interaction, $F(1,40)=0.49$, $p=.48$, $\eta_p^2=.01$. There was a main effect of relatedness, $F(1,40)= 6.76$, $p=.013$, $\eta_p^2=.14$, indicating higher performance for related (M=1.14; SD=0.75) compared with unrelated stimuli (M=0.94; SD=0.72). The two-way relatedness x group interaction was non-significant, $F(1,40)=1.32$, $p=.26$, $\eta_p^2=.03$, while the test x relatedness interaction was marginally significant, $F(1,40)=3.91$, $p=.054$, $\eta_p^2=.09$, with better performance for related (M=0.89; SD=0.71) compared with unrelated stimuli (M=0.52; SD=0.59) in the associative test (Tukey test, $p=.003$, Cohen's d=0.57), but not in the item test ($M_{related}=1.39$, SD=0.58 vs $M_{unrelated}=1.37$, SD=0.42) ($p=.99$, Cohen's d=0.05). Finally, the three-way test x relatedness x group interaction was not significant, $F(1,40)=0.01$, $p=.93$, $\eta_p^2=.01$.

[Figure 1 about here]

In order to assess whether AD patients had an associative memory deficit beyond their memory impairment for items, we conducted a linear regression analysis in which memory performance (indexed by *d'*) for unrelated pairs in the associative test was entered as outcome variable while item memory performance (*d'*) for items encoded in unrelated pairs and group were entered as first and second predictor, respectively. This analysis controlled for age, sex and education. Results revealed that memory performance for the item test did not significantly predict performance in the associative test, β=0.107, ΔR^2=.07, F(1,37)=3.01, *p*=.091. When group was added in second step, it marginally predicted associative memory performance for unrelated pairs, β=0.324, ΔR^2=.08, F(1,36)=3.70, *p*=.062, suggesting that healthy controls had greater associative memory performance than AD patients beyond their memory performance for the items forming these associations.

The 2 (group: control, AD) x 2 (test: item, associative) x 2 (relatedness: related, unrelated) repeated measures ANOVA on the response bias C revealed that the effect of group was not significant, F(1,40)=0.46, *p*=.50, η_p^2=.01, while there was a main effect of test, F(1,40)=45.51, *p*<.001, η_p^2=.53, with a more liberal bias in the associative (M=-0.25; SD=0.61) than in the item test (M=0.20; SD=0.50). The two-way group x test interaction was not significant, F(1,40)=1.86, *p*=.18, η_p^2=.04. There was a main effect of relatedness, F(1,40)=78.46, *p*<.001, η_p^2=.66, with a more liberal bias for related (M=-0.29; SD=0.49) than unrelated stimuli (M=0.23; SD=0.59). The two-way relatedness x group, F(1,40)=0.77, *p*=.38, η_p^2=.02, and test x relatedness interactions, F(1,40)=0.69, p=.41, η_p^2=.02, were not significant. There was however a significant test x relatedness x group triple

interaction, F(1,40)=5.67, *p*=.022, η_p^2=.12 according to which, in the associative test, patients had a more liberal bias for related (M=-0.54; SD=0.46) compared with unrelated pairs (M=0.20; SD=0.75) (Tukey test, *p*<.001, Cohen's d=1.19) while this difference was less important in controls ($M_{related}$=-0.53, SD=0.43 vs $M_{unrelated}$=-0.14, SD=0.44) (*p*=.006, Cohen's d=0.89).

One particular interest in the current study was to evaluate whether the variability in the ability to benefit from semantic prior knowledge among AD patients was related to the integrity of their semantic memory, especially for categorical relationships. Mean number of errors on each question type of the SKQ in patients and in controls are presented in Table 2.

[Table 2 about here]

First, number of errors on the SKQ was submitted to a 2 (group: control, AD) x 4 (question: Q1 (superordinate general), Q2 (superordinate intracategorical), Q3 (subordinate perceptual), Q4 (subordinate functional)) repeated-measure ANOVA. This revealed a main effect of group, F(1,40)=6.44, *p*=.015, η_p^2=.14, with more errors in patients (*M*=4.52, SD=2.75) than controls (*M*=2.67, SD=1.68), a main effect of question type, F(3,120)=20.81, *p*<.001, η_p^2=.34, with more errors for Q2 (*M*=1.31, SD=1.05), 3 (*M*=0.71, SD=0.83) and Q4 (*M*=1.48, SD=1.37) compared with Q1 (*M*= 0.12, SD=0.4), and a non-significant group x question type interaction, F(3,120)=0.92, *p*=.43, η_p^2=.02.

Second, to assess whether the degree of semantic memory alteration is related to participants' memory for related pairs, we conducted linear regression analyses with the *d'* for related and unrelated pairs as dependent variable and the total number of errors committed in the SKQ as predictor after controlling for the effects of age, sex and education. Error rates in the SKQ was a significant predictor of the *d'* for related pairs in controls (β=-0.498, ΔR^2=.20, F(1,16)=6.00,

p=.026), while it was not the case for unrelated pairs (β=-0.309, ΔR^2=.08, F(1,16)=1.55, *p*=.23). In patients, neither the regression between the number of errors in the SKQ and the *d'* score for related pairs (β=-0.265, ΔR^2=.05, F(1,16)=0.94, *p*=.35), nor the equivalent regression for unrelated pairs (β=0.02, ΔR^2=.00, F(1,16)=0.00, *p*=.99), were significant. So, in controls, but not in patients, the lower the number of errors on the SKQ, the better the discrimination performance for semantically related pairs.

Then, we evaluated more specifically whether superordinate categorical knowledge integrity was a significant predictor of memory performance as the associative memory task comprised categorical relationships. In controls, the number of errors to the questions that assessed categorical knowledge was a significant predictor of the *d'* for related pairs (β=-0.475, ΔR^2=.20, F(1,16)=6.15, *p*=.025)[1], while it was not the case for unrelated pairs (β=-0.057, ΔR^2=.01, F(1,16)=0.06, *p*=.82). In contrast, in AD patients, the regressions between the number of errors to superordinate categorical questions and *d'* for related and unrelated pairs were non-significant (β=-0.239, ΔR^2=.05, F(1,16)=0.98, *p*=.34, and β=-0.054, ΔR^2=.01, F(1,16)=0.05, *p*=.82, respectively). To sum up, a higher number of errors to superordinate categorical questions was associated with a lower categorically-related word pairs recognition in control participants, but not in AD patients.

Because knowledge about living things is more affected than knowledge about manufactured items in AD, we conducted finer analyses separating performance for living and non-living stimuli both in the SKQ and in the associative memory task. In the SKQ, the total number of errors was higher for living than non-living items in both patients (t(40)=-5.75, *p*<.001, Cohen's d=-1.82; M_{living}=3.86, SD=2.17; $M_{non\text{-}living}$=0.66, SD=1.31) and controls (t(40)=-5.86, *p*<.001, Cohen's d=-1.85; M_{living}=2.52, SD=1.78; $M_{non\text{-}living}$=0.19, SD=0.40). In the associative task, 2 (group: control, AD) x 3 (type of pair: unrelated, related living, related non-living) repeated-measure ANOVA on

[1] Note that the number of errors committed on other questions of the SKQ (superordinate general, subordinate perceptual and subordinate functional) did not significantly predict *d'* score for related pairs (all *p*s>.20).

hits-FAs[2] rates yielded a main effect of group, F(1,40)=18.84, p<.001, η_p^2=.32, reflecting better performance for controls (M=0.34; SD=0.27) compared with patients (M=0.14; SD=0.25). There was also a main effect of type of pair, F(2,80)=12.57, p<.001, η_p^2=.24, indicating better performance for related non-living pairs (M=0.39; SD=0.30) compared with related living (M=0.15; SD=0.27) (p<.001) and unrelated pairs (M=0.18; SD=0.20) (p<.001) that did not differ from each other (p=.84). The two-way group x relatedness interaction was not significant, F(2,80)=0.26, p=.77, η_p^2 =.01.

Because the number of errors on the SKQ to non-living objects was close to floor, and because patients' category deficit is thought to be specific to living things, further analyses were conducted on living concepts only. We conducted linear regression analyses with participants' discrimination performance (hits-FAs) for living pairs as dependant variable and the total number of errors on the SKQ for living items as predictor. Errors on the SKQ for living items were associated to performance for living word pairs in controls (β=-0.499, ΔR^2=.23, F(1,17)=5.81, p=.028), but not in patients (β=-0.023, ΔR^2=.00, F(1,17)=0.08, p=.93).

Discussion

This study assessed whether mild AD patients would benefit from semantic relatedness between words in associative memory, similar to healthy older adults. We further assessed whether this benefit was related to the integrity of semantic knowledge, with the hypothesis that AD patients should benefit from semantic relatedness to remember word pairs only when their semantic knowledge is preserved.

[2] The choice of using the « Hits-FAs » index instead of the *d'* was motivated by the limitation associated with the computation of the *d'* score, according to which 0 and 1 values need to be adjusted in order to compute the *d'*. In our case, such extreme values were too numerous when considering separately living and non-living stimuli, so that an adjustment would have biased the actual mean of discrimination performance.

Associative memory benefit from semantic relatedness

AD patients, like healthy older adults, displayed greater associative memory performance when word pairs were pre-experimentally related compared with when they were unrelated. However, for older participants, this improvement was not as important as in previous studies (Naveh-Benjamin et al., 2003; Patterson et al., 2009) in which the presence of a semantic link between words brought associative memory performance to the same level as item memory performance. This might be explained by the need for using recollection, a controlled, attention-demanding process that declines in healthy aging (Koen & Yonelinas, 2014), in order to reject recombined related word pairs formed by switching words between studied related pairs.

The same pattern of performance was observed in AD patients, although their general memory level was significantly poorer, which echoes with the existing literature showing that AD is accompanied by a severe episodic memory deficit (Bastin et al. 2014, Gallo et al. 2004). This deficit has notably been attributed to a decline in source monitoring processes (El Haj, Fasotti & Allain, 2012), a process that plays a role in associative recognition (Mitchell & Johnson, 2010) and that has been identified as a major factor contributing to the decline in source and destination memory observed in AD patients (El Haj, Moroni, Luyat, Omigie, & Allain, 2014; El Haj, Gely-Nargeot & Raffard, 2016). Interestingly, AD patients had a more liberal bias when discriminating related than unrelated word pairs while the difference was less important in healthy controls. This suggests that AD patients adopted a completely different response criterion depending on the type of word pairs considered. Related to this finding is the study of Balota, Burgess, Cortese and Adams (2002) that revealed that AD patients showed a more liberal bias for high frequency relative to low frequency words, perhaps because high frequency words are more familiar in an absolute way (Coane, Balota, Dolan & Jacoby, 2012). AD may thus be more likely than controls to adapt their decision criterion according to whether the word pair bears an absolute sense of familiarity or not. Nevertheless, even

if not spectacular, both groups improved their associative memory performance when words were related.

Interestingly, when dividing the related pairs between living and non-living related pairs, the improvement in associative memory for related pairs actually appeared to be driven specifically by non-living related pairs, while living related pairs were not better recognized than unrelated pairs in both patients and healthy older adults. Living concepts are thought to be more similar to one another because they share a greater number of features with less distinctive features than non-living concepts (Clarke & Tyler, 2015). It could thus be the case that relatedness within living pairs did not help improving the associative memory performance because recombined related living pairs were more similar to the target pair, and thus required finer discrimination, than related non-living pairs recombined with other non-living concepts. Previous studies indeed showed AD patients to experience difficulties in discriminating between close living concepts in an episodic memory task (Kivisaari, Monsch, & Taylor, 2013) and in a naming task (Kivisaari, Tyler, Monsch, & Taylor, 2012). Moreover, although only in the visual modality, some studies also showed fine discrimination impairments in healthy older adults (e.g., Ryan et al., 2012). Altogether, our results bring support to the theories according to which distinguishing between living concepts would require finer discrimination abilities than distinguishing between non-living ones (Clarke & Tyler, 2015).

Associative memory benefit from semantic relatedness and semantic knowledge integrity in healthy aging

It is widely accepted that semantic memory accumulates knowledge across the life span and remains relatively spared in healthy aging (Brickman & Stern, 2009; Drag & Bieliauskas, 2010) while it declines in AD (Chertkow et al., 2008; Laisney et al., 2010). The results of the SKQ fit with such a claim. Nevertheless, our results suggest that slight variations in semantic knowledge exist in healthy older adults. Moreover, the relation shown between these variations and performance in

associative memory for related pairs suggests that older adults' level of semantic knowledge could influence their performance in an episodic memory task where prior knowledge is manipulated. We suggest that older individuals' semantic knowledge might impact memory performance by determining, at least partially, the degree of elaboration at encoding (cf. Levels of Processing theory, Craik & Lockhart, 1972), therefore leading to a more or less successful discrimination at retrieval. These findings support hypotheses according to which one's capacity to efficiently use pre-existing semantic knowledge to support episodic learning is related to the integrity of one's semantic knowledge (Greenberg & Verfaellie, 2010). Consistent with this idea, Stevens-Adams, Goldsmith and Butler (2012), using the DRM paradigm, showed that the probability of committing a false alarm for a given lure was directly related to the structure and the development of semantic knowledge. More critically, this relationship occurred at the individual level suggesting that each individual processed each item differently in the memory task according to how his/her semantic network has been built-in throughout his/her life.

Associative memory benefit from semantic relatedness and semantic knowledge integrity in AD

Worthy of note is that our results in AD patients are discordant with a previous study that used the SKQ questionnaire in an AD population (Simoes Loureiro & Lefebvre, 2015). In that study, patients displayed worse performance for perceptual questions than intra-categorical ones while this was not the case in controls. In our study, patients displayed a similar pattern of performance as controls, although poorer, and did not display worse performance to perceptual than intra-categorical questions. This discrepancy in results might be explained by differences in age or education between the populations or the fact that our patients were at a mild stage of the disease, contrary to participants in Simoes-Loureiro and Lefebvre's study who ranged from a mild to a severe stage.

The fact that recognition of related pairs was not predicted by semantic knowledge integrity in AD patients could mean that they did not use their semantic knowledge – at least as measured by the SKQ – to perform the episodic memory task, contrary to healthy older adults. However, the improvement in patients' performance in the associative recognition task for related compared with unrelated pairs suggests that AD patients did use some residual semantic knowledge to support the encoding of related pairs. One possibility would be that the nature of the semantic information they used is different from the one assessed by the SKQ or the one used by control participants.

Alternatively, the lack of a relationship between the SKQ performance and memory for semantically related words may result from different modes of access to the information. Indeed, the SKQ may call on a controlled retrieval of semantic information within the semantic memory system, contrary to the associative memory task in which the access to the semantic content could be more automatically triggered by the presence of semantic relatedness. Consistently, controlled processes are typically more affected by mild AD than automatic processes (Bastin et al., 2010; Fabrigoule et al., 1998). Along those lines, it could be that the cognitive mechanisms that are involved in the two tasks of the current study (associative memory and SKQ) could be differently impaired in AD. Support for this interpretation comes from the study of Aronoff et al. (2006) that showed, in a same cohort of patients, that AD patients were as able as controls to identify that two related items (e.g. dog and cat) were conceptually close, while they had difficulties to access specific information about items taken individually. These findings suggest that whether AD patients demonstrate semantic memory deficits is determined by the way it is assessed. Thus, although the current associative memory task and the SKQ both involved categorical semantic information, one required to identify the categorical link between two words (associative memory), a capacity that was found preserved in AD, while the other necessitated to access semantic details relative to a single item (SKQ), an ability that is affected in AD (Aronoff et al., 2006).

Limitations and future directions

One limitation of the current study was the inequity in the target-lure proportion in the item recognition memory task that could have biased the calculation of global discrimination scores for this task. Moreover, a more systematic evaluation of semantic memory and of each of its mechanisms (semantic retrieval, semantic content, semantic regulation) should be included in future studies to help determining their contribution to episodic memory tasks by relating their respective integrity to performance. Relatedly, more detailed cognitive and functional evaluations of AD patients should be included to determine more precisely their dementia profile and to relate memory performance to other functions like executive abilities. Also, the sample size was relatively small but current results can be taken as a basis for sample size estimation to ensure sufficient power in future studies.

Another limitation is that the SKQ focuses on encyclopaedic knowledge, which may not be entirely representative of the integrity of semantic knowledge (i.e., one could understand the meaning of a word without mastering its encyclopaedic properties). Relatedly, future work should further explore the impact of semantic memory alteration in AD on the influence of prior knowledge on associative memory by assessing the perception of the relation between concepts rather than the knowledge for the concepts themselves, since these two measures lead to different conclusions with regard to patients' semantic alteration (Aronoff et al., 2006).

Finally, in addition to investigating whether semantic memory could bring support to participants' episodic memory, future research should assess whether these two memory systems could interact in a reverse fashion, with episodic memory influencing performance in a semantic task by providing an organizational framework that could guide semantic retrieval (e.g., generating birthday gifts examplars in a semantic task by referring to one's own experience of gifts received/offered, Greenberg, Keane, Ryan, & Verfaellie, 2009). Future work should assess

whether/how declining or impaired episodic memory influences how older adults and AD patients complete semantic knowledge evaluations.

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Tables

Table 1. Mean demographics and group differences.

	Controls (n=21)	**AD (n=21)**	**Group difference**
Age	76.95 (7.13)	76.52 (7.31)	t=-0.19, *p*= .84
M/F	9/12	12/9	
Education	11.24 (3.33)	11.14 (3.24)	t=-0.09, *p*=.92
Dementia Rating Scale	137.43 (3.19)	127.05 (9.12)	t=-4.75, *p*<.001

Table 2. Mean number of errors on each question type of the SKQ in controls and in patients

	Controls	Patients
Total	2.67 (1.68)	4.52 (2.75)
Q1	0.05 (0.22)	0.19 (0.51)
Q2	1.05 (0.74)	1.57 (1.25)
Q3	0.52 (0.51)	0.90 (1.04)
Q4	1.09 (1.18)	1.86 (1.46)

Figures

Figure 1. A) Discrimination performance (*d'*) in the item and associative recognition memory tests for control and AD participants as a function of relatedness conditions. B) Response bias (C) in the item and associative memory tests across groups and relatedness conditions. Each circle is a participant. Error bars represent the minimum and maximum points of the distribution, excluding outliers.

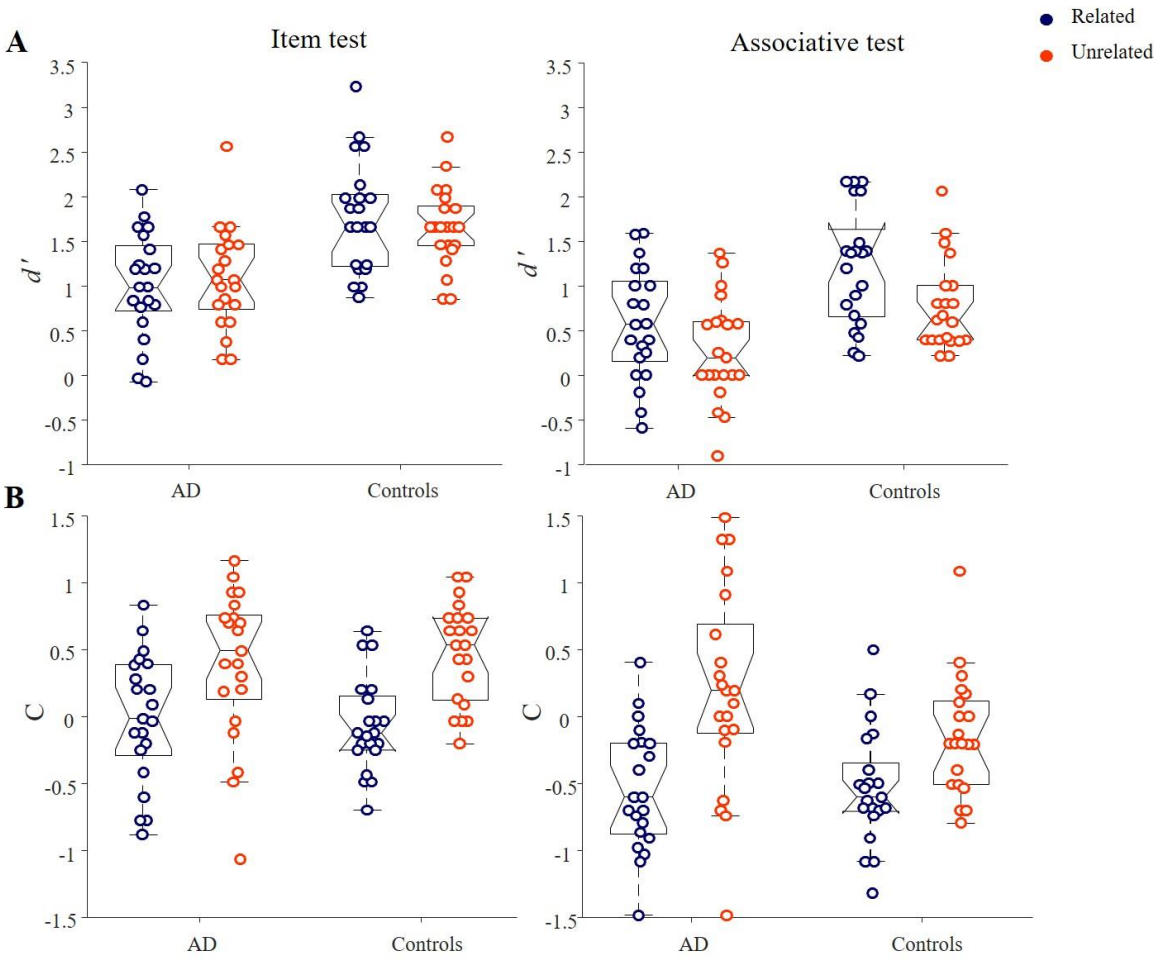

Figure 2. Linear regression analyses between the total number of errors committed in the SKQ and memory performance for related pairs (indexed by *d'*) in both groups. Each circle is a participant.