

Running title: recognition memory in Alzheimer's disease

Enhancing the salience of fluency improves recognition memory performance in mild  
Alzheimer's disease

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## Abstract

Recognition memory can rely on recollection (recall of the details from the encoding episode) and familiarity (feeling that some information is old without any recollection). In Alzheimer's disease (AD), whereas there is a clear deficit of recollection, the evidence regarding familiarity is mixed, with some studies showing preserved familiarity and others reporting impairment. The current study examined whether recognition memory performance can be improved in AD when the use of familiarity is facilitated by the salience of processing fluency due to an earlier encounter with the information. Fifteen AD patients and 16 healthy controls performed a verbal recognition memory task where the salience of fluency was manipulated by means of letters overlap. Studied and unstudied words were constituted of either two separate sets of letters (no-overlap condition, high fluency salience) or the same set of letters (overlap condition, low fluency salience). The results showed that, although performance was globally poorer in AD patients than in the controls, both groups performed significantly better in the no-overlap condition than in the overlap condition. This suggests that AD patients benefited as much as the controls from the salience of fluency.

Keywords: Alzheimer disease, episodic memory, recognition, familiarity.

## Introduction

Dual-process theories of recognition memory posit the existence of two independent kinds of memory (for a review, see [1]): recollection -the retrieval of specific details from the initial encounter with the information- and familiarity -a feeling of oldness devoid of any specific recall from encoding context. Whereas recollection is severely impaired in Alzheimer's disease (AD), the impact of this pathology on familiarity is less clear. Indeed, some studies reported preserved familiarity in AD [2-7], whereas others found that familiarity was impaired [8-13]. In order to understand the reasons for these conflicting findings and clarify whether familiarity is preserved or not in AD, it is important to explore the precise mechanisms that underpin familiarity-based responses in AD patients.

Familiarity is a complex function depending on the operation of several processes [14]. One important mechanism that has received much attention is the sense of familiarity driven by processing fluency, which is typically defined as enhanced speed and ease of processing due to an earlier encounter with the stimulus [15-22]. The conversion from fluency to familiarity is rooted in an inferential process, where the fluent processing of a previously encountered stimulus will be attributed to the fact that it is old. This attribution to prior occurrence leads to the consciously experienced sense of familiarity when fluency is perceived as relevant to the recognition decision [23-26]. So young adults do not experience a sense of familiarity when they are aware of the characteristics of the stimuli that explains why processing the items is especially fluent, such as when it is due to a manipulation of perceptual clarity of the stimuli [15, 23, 27] or when they experience fluency that they judge irrelevant to a recognition decision, such as visuo-perceptual fluency after auditory encoding [26].

In Alzheimer's disease, there is evidence that processing fluency can influence patients' recognition memory. First, previous research has shown that AD patients'

performance can be facilitated by prior perceptual processing of stimuli (perceptual priming), and under certain circumstances, by prior conceptual processing (see [28, 29] for reviews). Second, more direct evidence indicates that it is possible to induce false recognitions in mild AD patients by artificially enhancing perceptual or conceptual processing fluency at the time of test, for instance through masked visual priming [30] or by using a predictive conceptual context [5, 31, 32]. For example, AD patients are more likely to endorse as old the word “boat” (studied or not) if it is preceded by the predictive sentence stem “The stormy seas tossed the...” than if preceded by the non-predictive stem “She saved up her money and bought a...”. Moreover, similarly to healthy people, mild AD patients are also able to disregard fluency and do not experience familiarity when they feel that processing facilitation is not related to prior study [30], suggesting that metacognitive processes may be sufficiently preserved in mild AD patients to ensure control over the conversion from fluency to familiarity (for similar evidence, see [33]). Finally, the nature of the retrieval strategy used by AD patients may modulate whether or not they use available fluency cues [34]. Indeed, patients tend not to base their recognition decisions on fluency when they feel that the task constitutes a hard challenge, presumably because they cope with task difficulty by adopting an analytic processing. An analytic processing consists in isolating certain distinctive parts of the stimulus as potentially recognizable and promotes recollection-based recognition. Such an analytic strategy might block the experience of global processing fluency and thus the feeling of familiarity [19]. Importantly, we showed that instructions that modify how difficult the task is perceived by AD patients and induce a holistic processing of stimuli improved strikingly the patients’ recognition performance by promoting the reliance on fluency cues [34].

In order to further assess the capacity of patients with mild Alzheimer’s disease to benefit from fluency-based recognition, the current study examined whether an increase in the relevance and salience of fluency cues leads to an improvement of recognition performance in

AD. More precisely, given that fluency is intact and thus available as a cue for recognition in AD and that attribution processes seem also preserved, at least in the early stage of Alzheimer's disease [30], the use of fluency for recognition decisions could be enhanced by increasing its availability and salience. Such findings have been obtained in elderly participants [35] and in patients with amnesia [36]. In these experiments, studied and unstudied words derived either from two separate sets of letters (no-overlap condition) or from the same set of letters (overlap condition). In the no-overlap condition, exposure in the study phase induced both word and letter-level enhanced fluency for old stimuli. In contrast, in the overlap condition, the fluency for letters was equally present for old and new stimuli, so that old and new stimuli only differed on word fluency. In this context, although the absolute fluency of old items is likely equal in both conditions, the fluency difference between old and new stimuli (and thus the salience of fluency) is greater in the no-overlap condition than in the overlap condition. Parkin et al. [35] and Keane et al. [36] showed that increasing the salience of fluency by eliminating letter-level overlap between old and new stimuli significantly reduces the recognition deficit in elderly people and in patients with amnesia. Similarly, we hypothesized that increasing the salience of fluency should encourage AD patients to spontaneously adopt a fluency-based strategy to make recognition memory judgments. To date, one study examined the influence of letter fluency on recognition memory performance by means of the comparison between overlap and no-overlap conditions in Alzheimer's disease [37]. The results showed that AD patients failed to use letter fluency to improve memory. However, the dementia severity of patients from that study was already moderate, so that the failure of fluency-based familiarity could be due to the severity and extent of their cognitive deficits, potentially affecting attribution processes. Our study therefore focused on mild Alzheimer's disease, where fluency and attribution processes were previously found to be relatively intact [30].

## Materials and methods

### *Participants*

Fifteen patients diagnosed with probable Alzheimer's disease [38] (11 women) and 16 healthy elderly controls (12 women) were included. All participants gave their written informed consent to participate to the study which was approved by the ethics committee of the Faculty of Psychology of the University of Liège, according to the Declaration of Helsinki. Patients were recruited via memory clinics. Diagnosis was based on general examination, neurological and neuropsychological assessments and neuroimaging. Patients were included if their symptoms corresponded to a mild stage of AD, as indicated by a MMSE score above 20 [39]. A characteristic pattern of cerebral hypometabolism (FDG-PET) was taken as biomarker. Healthy controls had no neurologic or psychiatric problems, were free of medication that could affect cognition, and reported being in good health. The AD and control groups were matched in terms of age (AD:  $76.8 \pm 5.3$ , controls:  $77.7 \pm 5.2$ ,  $t(29) = 0.46$ ,  $p > .46$ ) and number of years of education (AD:  $10.1 \pm 2.4$ , controls:  $9.4 \pm 2.6$ ,  $t(29) = -0.68$ ,  $p > .49$ ). On the Mattis Dementia Rating Scale [40], AD patients' scores ranged from 113 to 133 ( $125.6 \pm 5.3$ ) out of 144, whereas the controls scored from 133 to 142 ( $137.7 \pm 3.0$ ). The patients scored poorer than the controls,  $t(29) = 7.88$ ,  $p < .001$ .

### *Materials*

The stimuli consisted of 120 French nouns. The mean frequency per 100 million (according to the Brulex database [41]) was  $1573 \pm 2158$ . Half of the words belonged to the no-overlap condition and the other half to the overlap condition. In the no-overlap condition, the 60 words were made of 30 words composed of a subset of letters of the alphabet (a, b, d, g, l, n, o, r, t, v, w, y, z) and 30 words composed of the remaining letters (c, e, f, h, i, j, k, m, p, q, s, u, x). In contrast, the 60 words in the overlap condition were based on the whole alphabet and

had to contain at least one letter from the two subsets of letters used in the no-overlap condition. Words in the overlap condition were randomly divided in two lists of 30 words. Each letter appeared equally frequently in both lists.

The four resulting word lists (2 lists in the no-overlap condition and 2 lists in the overlap condition) were matched in terms of length, lexical frequency and phonotactic frequency [41]. In each condition, the two lists of 30 words served to create a yes/no recognition task. At encoding, 30 words were presented. At test, stimuli consisted of the 30 studied words mixed with 30 non-studied words. Within each condition, the status of each list as target and as distractor was counterbalanced across participants.

The stimuli were presented in a booklet in which each word was printed at the center of a sheet of paper, in Times New Roman police, size 36.

### *Procedure*

Participants were tested individually and performed both the no-overlap and overlap recognition tasks. The order of presentation of the conditions was rotated across participants. In each condition, the study phase involved the presentation of 30 words at a rate of one word every 2 sec. Participants were instructed to read the words aloud and to try and remember them. The retention interval of 4 min was filled with open/closed judgments for geometrical figures for 2 min [42] and simple arithmetic problems for the remaining 2 min. At test, the 30 studied words randomly mixed with 30 new words were presented one at a time. Participants had to indicate whether the words were previously presented or not (yes/no judgments). Responses were self-paced. A delay of 2 minutes filled with conversation separated the two recognition tasks.

### Results

The proportions of hits and false alarms for each group and in each condition are presented in Table 1. An analysis of variance (ANOVA) with group (AD vs. control) as between-subject variable and condition (no-overlap vs. overlap) as repeated measure was performed on the scores. AD patients made significantly less hits than controls,  $F(1, 29) = 12.05$ ,  $\eta^2_p = 0.29$ ,  $p < .01$ . Both groups recognized more targets in the no-overlap condition than in the overlap condition,  $F(1, 29) = 14.6$ ,  $\eta^2_p = 0.33$ ,  $p < .001$ . The interaction was not significant,  $F < 1$ . As for false alarms, they were more frequent in the AD group than in the control group,  $F(1, 29) = 8.16$ ,  $\eta^2_p = 0.21$ ,  $p < .01$ . There were also more false alarms in the overlap condition than in the no-overlap condition,  $F(1, 29) = 10.17$ ,  $\eta^2_p = 0.25$ ,  $p < .01$ . There was no group by condition interaction,  $F < 1$ .

The ability to discriminate between targets and distractors was explored by the signal detection measure  $d'$  [43] (Figure 1). An ANOVA on  $d'$  scores indicated that recognition accuracy was poorer in the AD group than in the control group,  $F(1, 29) = 24.12$ ,  $\eta^2_p = 0.45$ ,  $p < .001$ , and also poorer in the overlap condition than in the no-overlap condition,  $F(1, 29) = 16.23$ ,  $\eta^2_p = 0.35$ ,  $p < .001$ . The group by condition interaction was not significant,  $F < 1$ . Furthermore, response bias was measured by the criterion  $c$  (see Table 1). An ANOVA on  $c$  scores did not reveal any significant effect (all  $F_s < 1$ ).

## Discussion

In order to clarify the status of familiarity-based recognition memory in mild Alzheimer's disease, this study examined the integrity of one of the mechanisms underlying familiarity memory. More specifically, healthy individuals experience familiarity when the enhanced fluent processing of a previously encountered stimulus is attributed to its prior occurrence [20, 23, 24]. Previous work suggested that AD patients can rely on fluency cues to make memory decisions. Several studies have shown this effect on false recognition. More precisely, when



fluency is artificially enhanced, patients' recollection deficit prevents them from counteracting feelings of familiarity, thus inducing incorrect endorsement of unstudied items [5, 31]. However, reliance on fluency can also improve correct recognition responses [44]. Here, we tested whether AD patients can benefit as well as healthy controls from pertinent fluency cues (i.e., cues that allow to discriminate between old and new items) in their memory decisions when these cues are made more salient [45].

In the current study, the salience of fluency cues was manipulated by increasing the relative fluency processing between old and new words by using different sets of letters for each type of words. Consistently with previous studies showing that enhancing sublexical fluency allow more accurate recognition performance in memory-impaired populations [35, 36], the current findings indicated that, despite their global impairment of recognition memory, AD patients benefited from the enhancement of fluency salience to the same extent as healthy controls and significantly improved their ability to discriminate between old and new words when there is no letter overlap between the two categories of items. This memory improvement manifested itself as an increase in hits and a decrease in false alarms in the no-overlap condition.

These results contrast however with the failure of AD patients to benefit from enhanced sublexical fluency in a previous study [37]. There are two possible and nonexclusive explanations for this discrepancy in findings. First, as the study by Algarabel et al. [37] involved more severe patients, the absence of enhanced fluency-based recognition memory could be due to the severity of the patients' cognitive deficits. More particularly, the use of fluency as a cue for recognition memory depends on metacognitive attribution processes. Kurilla and Gonsalves [46] and Wolk et al. [25] observed that these processes correlated with a frontal-based event-related potential (ERP) component, which is known to be associated with post-retrieval monitoring processes [47]. Importantly, pathological changes

in the prefrontal cortex have been reported in Alzheimer's disease, especially in more severe patients [48, 49]. Therefore, it may be that frontal lobe dysfunction in patients in a moderate stage of dementia caused impaired post-retrieval monitoring processes, leading these patients to sub-attribute fluency to prior occurrence of the item. In the current study, patients may have still been able to use attribution processes given their milder stage of dementia. Second, the materials in Algarabel et al.'s study involved words with a higher lexical frequency than the words used here. Indeed, the words used by Algarabel et al. had a mean frequency of 31.5 per million in contrast to 16 per million here. Higher word frequency could influence performance in two ways. First, increasing the frequency of all words in a memory task enhances also the global fluency context (fluency for items independently of studied or unstudied status), which comes from prior encounters with the words outside the experimental context and thus decreases the salience of exposure-related fluency [50]. Second, a single exposure increases the effective fluency of higher frequency words to a smaller extent than fluency of lower frequency words [51]. Therefore, the lower frequency of the words used in our study may have contributed to enhance the salience of fluency even further in the case of non-overlapping letters, thus creating conditions where fluency cues are particularly relevant to make recognition judgments. This possibility should be explored in future studies.

Of note, in the current study, both AD patients and healthy controls demonstrated a conservative response bias, which was not affected by the fluency manipulation. These findings contradict the frequent observation that AD patients show an abnormally liberal response bias independently of poorer discrimination abilities [10, 52]. Moreover, enhancing patients' reliance on fluency was often found to shift them to a more liberal response bias [5, 32]. Although it remains unclear what determines the response bias adopted by AD patients, it seems that, in certain conditions, they are not biased towards "yes" answers or even show conservative criteria [44, 53, 54]. One such condition, relevant to the current study, is the

frequency of verbal stimuli. Indeed, healthy older adults as well as AD patients showed a more conservative response bias (also close to 0.20 as here) for low frequency words than for high frequency words [55]. The greater pre-experimental familiarity of high frequency words may increase the tendency of patients, likely to rely on familiarity, to respond “old” to both targets and distractors. Moreover, Budson et al. [10] suggested that the degree of AD pathology may influence the patients’ bias, with more liberal bias in more severely affected patients. Additionally, in a mixed group of patients with AD or frontotemporal lobar degeneration, smaller frontal volumes were associated with a more liberal response bias [56]. It may therefore be that a combination of characteristics of the patients and the experimental task explained the adoption of a conservative response bias in the current sample.

Finally, although enhancing the salience of fluency cues significantly improved recognition accuracy in AD patients, this did not reduce the amplitude of their memory deficit. Healthy participants typically rely on a mixture of recollection-based and familiarity-based memory decisions. The manipulation of fluency is assumed to improve familiarity-based discrimination in both AD patients and healthy controls, but the severe deficit of recollection that characterized the patients will prevent their performance from reaching the same level as controls. Moreover, it may be necessary to combine manipulation of perceptual and conceptual fluency to attenuate the recognition deficit in mild AD. Indeed, when patients with mild AD rely on both conceptual and perceptual information for recognition decisions, accuracy is improved compared to relying on either type of information alone [32, 44].

In order to directly relate the benefit of enhancing the salience of fluency to the integrity of familiarity processes in mild Alzheimer’s disease, future work needs to combine the current manipulation of sublexical fluency to estimates of the contribution of recollection and familiarity. In amnesic Mild Cognitive Impairment, a recent study reported preserved familiarity during recognition of pictures and impaired familiarity during recognition of words

[57]. This picture superiority effect was interpreted as resulting from enhanced perceptual and/or conceptual fluency due to distinctive visual information. In a similar vein, we hypothesize that, in mild AD, familiarity-based memory should appear preserved in conditions where fluency cues are sufficiently discriminant and salient to be used by the patients. In contrast, familiarity-based memory may be impaired when fluency cues are misleading and should be countered by recollection or when participants adopt a processing strategy that leads them to favor recollection and disregard fluency cues.

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Table 1. Mean proportions of hits, false alarms and response bias (c) in the No-overlap and Overlap conditions in the AD group and the Control group.

Condition	AD			Control		
	Hits	False alarms	C	Hits	False alarms	C
No-overlap	.65 (.13)	.22 (.16)	.25 (.49)	.79 (.11)	.11 (.07)	.21 (.45)
Overlap	.61 (.13)	.28 (.15)	.20 (.49)	.76 (.10)	.15 (.08)	.18 (.35)

Standard deviations are in parentheses.

Figure legends

Figure 1. D-prime scores as a function of Group and Condition

Figure 1

