

Patients with mild Alzheimer's disease attribute conceptual fluency to prior experience

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Abstract

Patients with Alzheimer's disease (AD) have been found to be relatively dependent on familiarity in their recognition memory judgments. Conceptual fluency has been argued to be an important basis of familiarity. This study investigated the extent to which patients with mild AD use conceptual fluency cues in their recognition decisions. While no evidence of recognition memory was found in the patients with AD, enhanced conceptual fluency was associated with a higher rate of "Old" responses (items endorsed as having been studied) compared to when fluency was not enhanced. The magnitude of this effect was similar for patients with AD and healthy control participants. Additionally, ERP recordings time-locked to test item presentation revealed preserved modulations thought critical to the effect of conceptual fluency on test performance (N400 and late frontal components) in the patients with AD, consistent with the behavioral results. These findings suggest that patients with mild AD are able to use conceptual fluency in their recognition judgments and the neural mechanisms supporting such processing is maintained.

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1. Introduction

Dual-process accounts of recognition memory posit that *familiarity* and *recollection* are distinct memory processes (Gardiner, 1988; Jacoby, 1991; Mandler, 1980) [for review see Yonelinas, 2002]. Recollection is often described as the detailed retrieval of information regarding an item or event, including the context in which it was experienced, while familiarity is thought to represent a general sense of prior encounter.

Patients with Alzheimer's disease (AD) have significant episodic memory impairment due to extensive pathological involvement of the medial temporal lobes. As with am-

nesic patients with medial temporal lobe injury (Aggleton & Shaw, 1996; Knowlton & Squire, 1995; Schacter, Verfaellie, & Anes, 1997; Schacter, Verfaellie, & Pradere, 1996; Yonelinas, Kroll, Dobbins, Lazzara, & Knight, 1998), several studies have suggested that patients with AD have more significant impairment of recollection-based than familiarity-based recognition (Budson, Desikan, Daffner, & Schacter, 2000; Christensen, Kopelman, Stanhope, Lorentz, & Owen, 1998; Dalla Barba, 1997; Gallo, Sullivan, Daffner, Schacter, & Budson, 2004; Knight, 1998; Koivisto, Portin, Seinela, & Rinne, 1998; Smith & Knight, 2002). For example Budson et al. (2000) employed a manipulation originally developed by Deese (1959) and modified by Roediger and McDermott (1995), which involves studying a list of semantic associates (e.g., *candy*, *sour*, *sugar*, *bitter*, *good*, *taste*, etc.) that converge on an unrepresented "related lure" (e.g., *sweet*). At test,

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subjects are presented with previously studied words, related lures, and novel items. Although normal controls demonstrated a high false alarm rate to related lures, they were still more likely to endorse studied words as “Old” than related lures. This discrimination improved with repeated study-test trials. In contrast, patients with AD demonstrated no discrimination between these item types (i.e. true recognition = false recognition). Because true recognition is thought to be supported by both recollection and familiarity while false recognition to related lures is thought to be supported by familiarity and opposed by recollection, these data suggest that patients with AD were reliant solely on familiarity in their responding. Thus, as suggested by this study and others, future investigation of the neuropsychological and underlying brain processes supporting familiarity is of particular relevance to this population.

Previous work has suggested that an important basis for familiarity is related to the ease with which an item is processed, also referred to as its processing *fluency* (Jacoby & Whitehouse, 1989; Kelly & Jacoby, 2000; Rajaram & Geraci, 2000; Westerman, 2001; Whittlesea, 1993; Whittlesea & Williams, 2000, 2001a, 2001b) [but see (Higham & Vokey, 2004)]. This notion stems from the phenomenon that prior presentation of an item leads to easier identification when that item is re-presented in a degraded fashion (Jacoby & Dallas, 1981). Thus, when making recognition judgments, enhanced processing fluency could be used by the subject as a cue that an item was previously studied (Jacoby & Dallas, 1981; Jacoby & Whitehouse, 1989; Kelly & Jacoby, 2000; Whittlesea, 1993; Whittlesea, Jacoby, & Girard, 1990). In support of this view, manipulations that alter perceptual fluency, such as varying the visual clarity of test items, influence how subjects respond on tests of recognition memory. More fluent (or easier to perceive) items are more likely to be endorsed as being on a prior study list than less fluent items (Jacoby & Whitehouse, 1989; Whittlesea et al., 1990).

Similarly, manipulations of *conceptual fluency* (the ease of conceptual processing) can also influence recognition memory judgments (Rajaram & Geraci, 2000; Whittlesea, 1993; Whittlesea & Williams, 2000, 2001a, 2001b). When test words are preceded by a conceptually predictive context, subjects are more likely to endorse these items as previously studied than when preceded by a non-predictive context (Whittlesea, 1993; Whittlesea & Williams, 2001a). For example, subjects are more likely to say that the word “boat” was on a study list if it follows the predictive sentence stem, “The stormy seas tossed the. . .” than the non-predictive stem, “She saved up her money and bought a. . .” The predictive context, as a semantic prime, is thought to enhance the ease of conceptual processing, which is then mistaken as a cue of prior study.

However, fluency alone does not determine recognition judgments; enhanced fluency must also be *attributed* to prior experience (Jacoby & Whitehouse, 1989; Whittlesea et al., 1990; Whittlesea & Williams, 2001a). In other words, enhanced fluency does not result in an increased rate of endorsing items as previously studied unless the subject feels that

this enhancement is related to prior study, and not to an alternative source. For example, if subjects are aware that fluency is being experimentally manipulated, fluency no longer impacts recognition judgments (Jacoby & Whitehouse, 1989; Whittlesea et al., 1990). Thus, in the setting of enhanced fluency, processing involved in assessing whether or not to attribute this enhancement to prior experience is critical to the effect of fluency on recognition judgments. Indeed, it may be this attributional process which determines whether fluency produces a conscious experience of familiarity (Whittlesea & Williams, 2001a, 2001b).

Despite the apparent reliance on familiarity-based processing in patients with AD and the relationship of fluency to such processing, there have been no studies examining the impact of manipulations of fluency on these patients. Indeed, there has been only one investigation in patients with amnesia directly examining the impact of such manipulations. In this study, Verfaellie and Cermak (1999) found that patients with amnesia were more dependent than control subjects on manipulations of fluency in their recognition performance. Thus, fluency appears of particular salience in the recognition judgments of memory-impaired populations.

The current study was performed to investigate (1) whether patients with mild AD use conceptual fluency as a cue in their recognition judgments and (2) the effect of AD on the neural correlates of this activity. In order to do so, we employed the manipulation developed by Whittlesea and colleagues of having test words preceded by either predictive or non-predictive sentence stems in a recognition memory paradigm. As a reflection of the relative sparing of familiarity-based recognition and the relationship of fluency with familiarity-based processing, we hypothesized that patients with AD would be influenced by this manipulation, demonstrating a greater likelihood to endorse items following a predictive context as previously studied relative to those following a non-predictive context. We predicted that this effect would be larger for the patients than the controls, consistent with prior work demonstrating a greater dependence on fluency cues in the setting of weak memory (Johnston, Hawley, & Elliot, 1991; Verfaellie & Cermak, 1999; Westerman, Lloyd, & Miller, 2002; Westerman, Miller, & Lloyd, 2003).

In order to gain further insight into the underlying brain processes supporting the use of fluency cues in relation to Alzheimer’s disease, we recorded event-related potentials (ERPs). ERPs are scalp recordings of brain activity that are time-locked to experimental stimuli and responses. The various positive and negative fluctuations, referred to as ERP “components”, are thought to reflect specific sensory, perceptual, and cognitive processes (Rugg & Coles, 1995). Through analysis of these components processing differences based on the stimulus presented or the response given can be determined.

In previous work, we recorded ERPs in young adult subjects using the same conceptual fluency manipulation as the current study (Wolk et al., 2004). We found that enhanced fluency (words following a predictive context) produced at-

tenuation of the N400 component. In studies of language the N400 has been shown to be modulated by semantic expect- edness or the ease with which an item is semantically inte- grated into its context (Holcomb, 1993; Kutas & Hillyard, 1980; Rugg & Doyle, 1994). This *ease* of semantic integra- tion may be construed as analogous to processing fluency.¹ Critically, the N400 attenuation we found associated with en- hanced fluency was not associated with the subjects' recog- nition response ("Old" or "New"). This result is consistent with the notion that fluency does not itself dictate response, but is the substrate upon which attributional processing is per- formed. Indeed, in the setting of enhanced fluency we found a later (1200–1600 ms), frontally maximal modulation that was associated with whether or not an item was endorsed as studied. We proposed that this late frontal activity repre- sented processing involved in making attributions of fluency. As other studies involving recognition judgments have found late frontal modulations thought to reflect prefrontal activity involved with the evaluation of the contents of memory, or *post-retrieval processing* (Goldmann et al., 2003; Nessler et al., 2001; Ranganath & Paller, 2000; Wilding, Doyle, & Rugg, 1995; Wilding & Rugg, 1996, 1997a, 1997b), we posited that attributions of fluency may fall within this class of activity.

In the present investigation, we were interested in the im- pact of AD on both of these critical ERP components (N400 and late frontal) involved in the processing of conceptual fluency in recognition memory judgments. If, as we predicted, the impact of fluency is maintained in patients with mild AD, these components would be expected to be relatively pre- served. However, if the use of fluency cues is impaired in AD, this would be expected to be reflected electrophysiologically in diminution of either or both of these modulations, provid- ing insight into the underlying nature of this impairment.

2. Methods

2.1. Subjects

Informed consent was obtained in 12 subjects with the diagnosis of probable AD [using the National Institute of Neurological and Communicative Disorders and Stroke- Alzheimer's Disease and Related Disorders Association cri- teria (McKhann, Drachman, Folstein, Katzman, & Price, 1984); eight male] and 12 healthy control subjects (six male). Patients with AD were recruited from the Memory Disorders Unit at Brigham and Women's Hospital (Boston, MA) and older adults from the surrounding community. The

subjects were matched on the basis of age (patients with AD $M = 71.8$ years, range = 55–80; controls $M = 75.0$ years, range = 65–86; $t(22) = 1.044$, $p = 0.31$) and years of educa- tion (patients with AD $M = 16.4$ years, range = 12–23; con- trols $M = 15.9$, range = 12–21; $t(22) < 1$). Subjects were ex- cluded on the basis of clinical depression, alcohol or drug use, significant cerebrovascular disease, traumatic brain dam- age, or primary language other than English. As we wanted to study mild patients, patients were excluded if their Mini- Mental Status Examination (MMSE; Folstein, Folstein, & McHugh, 1975) was less than 20. On average, control sub- jects scored higher than subjects with AD on the MMSE (patients with AD $M = 25.1$, S.D. = 3.2; controls $M = 29.3$, S.D. = 0.8; $t(22) = 4.542$, $p < 0.001$). Control subjects also re- called more items on the delayed recall portion of the CERAD [(Morris et al., 1989); patients with AD $M = 1.1$, S.D. = 1.5; controls $M = 6.7$, S.D. = 1.8; $t(21) = 8.200$, $p < 0.0000001$; one control subject did not perform this test]. Lexical fluency to letters (F-A-S) and categories [(animals, fruits, and vegetables); (Salmon & Butters, 1992)] also resulted in sig- nificantly better performance in the control group (letters: patients with AD $M = 37.6$, S.D. = 13.1; controls $M = 50.4$, S.D. = 8.5; $t(21) = 2.85$, $p < 0.01$; categories: patients with AD $M = 28.4$, S.D. = 11.5; controls $M = 45.5$, S.D. = 9.1; $t(21) = 4.04$, $p = 0.001$). All participants were paid \$25/h. The study was approved by the human subjects committee of Brigham and Women's Hospital.

2.2. Stimuli

The stimuli were adapted and expanded from Whittlesea and Williams (2001a). Each of 240 one-syllable words was matched with a pair of sentence stems, one that predicted the word (predictive context) and the other that was merely consistent with it (non-predictive context). For example, for the word "rake" the sentence stems "To remove the leaves she used a" and "He clumsily tripped over the" represent typical predictive and non-predictive contexts respectively.

2.3. Procedure

The study session was self-paced; participants were asked to count aloud the number of "e"s in 120 visually presented, upper-case words. After each verbal response, the experi- menter advanced to the next word. At test, 120 studied and 120 non-studied words were presented in a pseudo-random order in both the visual (lower-case) and auditory modalities for recognition judgment. Sixty studied and 60 non-studied words were preceded by a predictive context; the other 60 studied and 60 non-studied words were preceded by a non- predictive context. Sentence stems were also presented in the visual and auditory modalities. Auditory presentation as- sured that the patients with AD would have at least heard each sentence stem if limited by slow reading. Four study- test lists were counterbalanced by study and context type. Sentence stem presentation time varied based on the audi-

¹ It is noteworthy that the putative ERP correlate of familiarity in recog- nition memory studies shares a number of characteristics with the N400 of language studies, although often with a somewhat more anterior distribution (Curran & Cleary, 2003; Duzel, Yonelinas, Mangun, Heinze, & Tulving, 1997; Finnigan, Humphreys, Dennis, & Geffen, 2002; Nessler, Mecklinger, & Penney, 2001; Rugg et al., 1998). This relationship suggests a further link between the neural generators of fluency and familiarity.

tory presentation. The following sequence followed the offset of the sentence stem: a pause (250 ms); the sentence final word (1000 ms), 500 ms pause, and finally an “Old or New?” prompt. Subjects were told that “Old” responses indicated that they thought the word was on the previous study list while “New” responses indicated that they did not. Subjects were told to refrain from responding until this prompt appeared. The subjects’ verbal response was entered by the experimenter. A “+” sign appeared for 1000 ms marking the start of the next trial.

2.4. Electrophysiological recording

ERPs were recorded at test from nine scalp sites referenced to the left mastoid: five midline (FPz, Fz, Cz, Pz, Oz) and four lateral (F3, F4, P3, P4). These were sites of interest based on our prior work in healthy young subjects (Wolk et al., 2004). Electrodes were placed below the left eye (LE), the lateral canthi of both eyes (HE), and FP1 to monitor for blinks and horizontal eye movements. The ERPs were amplified (0–40 Hz, SAI BioAmplifier system), and the recorded data were digitized (100 Hz) beginning 100 ms before onset of the test word. Trials were analyzed for 1600 ms following stimulus presentation. Trials with amplifier blocking or eye movements were excluded; blinks were corrected (Dale, 1994). Only ERPs formed from 16 or more artifact free trials were accepted for analysis (Wilding & Rugg, 1997b).

2.5. ERP analyses

The mean amplitude (relative to a 100 ms pre-stimulus baseline) for the two intervals of interest were calculated: 325–625 and 1200–1600 ms. The former was chosen to examine the N400 and the latter to evaluate the impact of the late frontal effect. Our prior study of undergraduates found (1) N400 attenuation associated with enhanced fluency (items following a predictive context); and (2) late frontal modulation (1200–1600 ms) associated with the subjects’ response in the setting of enhanced fluency, but not in the unenhanced condition (items following a non-predictive context; Wolk et al., 2004). In light of these findings, we analyzed both latencies with respect to these contexts. Only midline sites were analyzed, as there were no effects of laterality with any of the main conditions examined. Data from Cz and Oz were averaged to generate Pz in one control subject due to electrode failure. For analysis of the ERP data, the Greenhouse-Geisser correction procedure was used for repeated measures factors with greater than one numerator degree of freedom. Main effects of site and non-significant interactions are not reported unless of theoretical significance.

3. Results

3.1. Behavioral data

For a summary of the behavioral results, see Table 1. As expected, the control subjects exhibited greater accuracy in

Table 1

Mean proportion of “Old” responses and signal detection data for patients with AD and controls

	Studied	Non-studied	d'	C
Controls				
Non-predictive	0.48 (0.03)	0.34 (0.03)	0.39 (0.04)	0.24 (0.08)
Predictive	0.56 (0.03)	0.43 (0.03)	0.34 (0.06)	0.01 (0.08)
All	0.52 (0.03)	0.38 (0.03)	0.36 (0.03)	0.13 (0.08)
Patients with AD				
Non-predictive	0.41 (0.02)	0.39 (0.02)	0.06 (0.04)	0.25 (0.05)
Predictive	0.51 (0.03)	0.48 (0.03)	0.07 (0.09)	0.01 (0.07)
All	0.46 (0.02)	0.44 (0.02)	0.06 (0.04)	0.13 (0.05)

S.E.M. in parentheses.

their recognition judgments than the patients with AD, who were unable to discriminate studied from non-studied items. However, fluency appeared to impact both groups to a similar extent; both studied and non-studied items following a predictive context were more likely to be endorsed as “Old” than items following a non-predictive context.

An item type (studied, non-studied) \times context type (predictive, non-predictive) \times group (controls, patients with AD) ANOVA revealed an effect of item type [$F(1,22) = 54.14$, $p < 0.000001$] with studied items being called “Old” more often than non-studied items (0.49 versus 0.41) and an effect of context type [$F(1,22) = 45.66$, $p < 0.000001$] with items following a predictive context more often called “Old” than items following a non-predictive context (0.50 versus 0.41). There was an interaction of item type \times group [$F(1,22) = 25.43$, $p < 0.0001$], which was attributable to the controls endorsing more studied items as “Old” than non-studied items [$F(1,11) = 105.18$, $p < 0.000001$] whereas patients with AD did not [$F(1,11) = 2.11$, $p = 0.17$]. Thus, as reflected by the rate of “Old” endorsements for studied and non-studied items, patients with AD were unable to differentiate these item types (0.46 studied versus 0.44 non-studied) while controls were able to do so (0.52 studied versus 0.38 non-studied). There were no other interactions. Notably, there was not a group \times context type interaction [$F(1,22) < 1$], suggesting a similar effect of fluency on the responding of both groups.

Signal detection measures of d' (discrimination) and C (bias) were calculated (see Table 1). For d' , a context type (predictive, non-predictive) \times group (controls, patients with AD) ANOVA revealed no effect of context type [$F(1,22) < 1$] or context type \times group interaction [$F(1,22) < 1$]. There was an effect of group [$F(1,22) = 27.90$, $p < 0.0001$], indicating that the patients with AD had poorer discrimination ($d' = 0.06$) than the controls ($d' = 0.36$). The same ANOVA was performed for C and revealed a main effect of context type [$F(1,22) = 47.78$, $p < 0.000001$], reflecting a greater bias to categorize items following a predictive context as “Old” ($C = 0.01$) than items following a non-predictive context ($C = 0.24$). There were no interactions.

As prior work has suggested that subjects with poor memory are more likely to rely on fluency cues for their recogni-

tion judgments (Verfaellie & Cermak, 1999), we determined the correlation of discrimination with the *fluency effect*, which we defined as the percent of “Old” responses to items following a predictive context minus the percent following a non-predictive context. Consistent with this hypothesis, a significant Pearson correlation was found for the controls ($r = -0.60, p = 0.039$); poorer discrimination was associated with a larger fluency effect. This correlation was not found for the patients with AD ($p > 0.1$) likely because the discrimination of patients was close to zero for all participants. There were no significant correlations between the fluency effect and any other neuropsychological measure tested (MMSE, F-A-S, categories, or CERAD) in the patients with AD, with only F-A-S approaching significance ($r = 0.52, p = 0.100$).

3.2. ERP analysis

ERPs from this study are presented in Figs. 1 and 2. Fig. 1 shows averaged data at parietal sites based on context type (predictive, non-predictive), collapsed across item type (studied, non-studied), and Fig. 2 shows ERPs based on context type (predictive, non-predictive) and subject response (“Old” or “New”). An N400 is present in both groups and appears of lower voltage in the patients than controls (Figs. 1 and 2). Both groups also exhibit frontal modulations from approximately 1000–1200 ms until the end of the recording epoch associated with response (“Old” or “New”) in the enhanced fluency condition (items following a predictive context). This

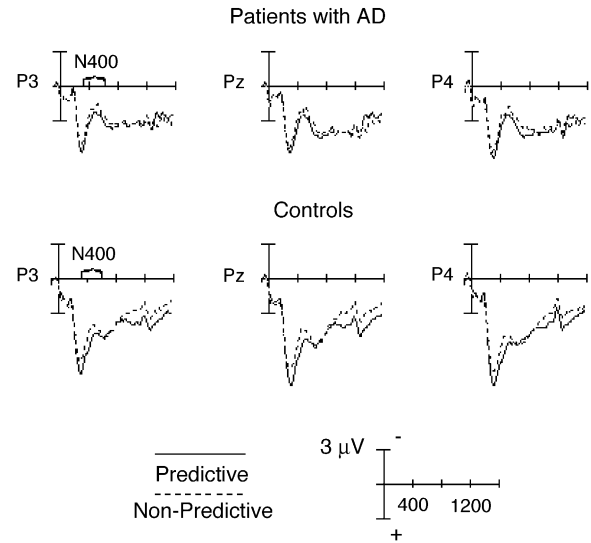


Fig. 1. Grand average ERP plots for three parietal sites (P3, Pz, P4). ERPs of items (studied and non-studied) following predictive and non-predictive contexts. The top tracings are of the patients with AD and the bottom are of the controls.

modulation is reduced in both groups for items following a non-predictive context (Fig. 2).

3.2.1. N400

Mean ERP amplitude (325–625 ms) was calculated for predictive–studied, non-predictive–studied, predictive–non-

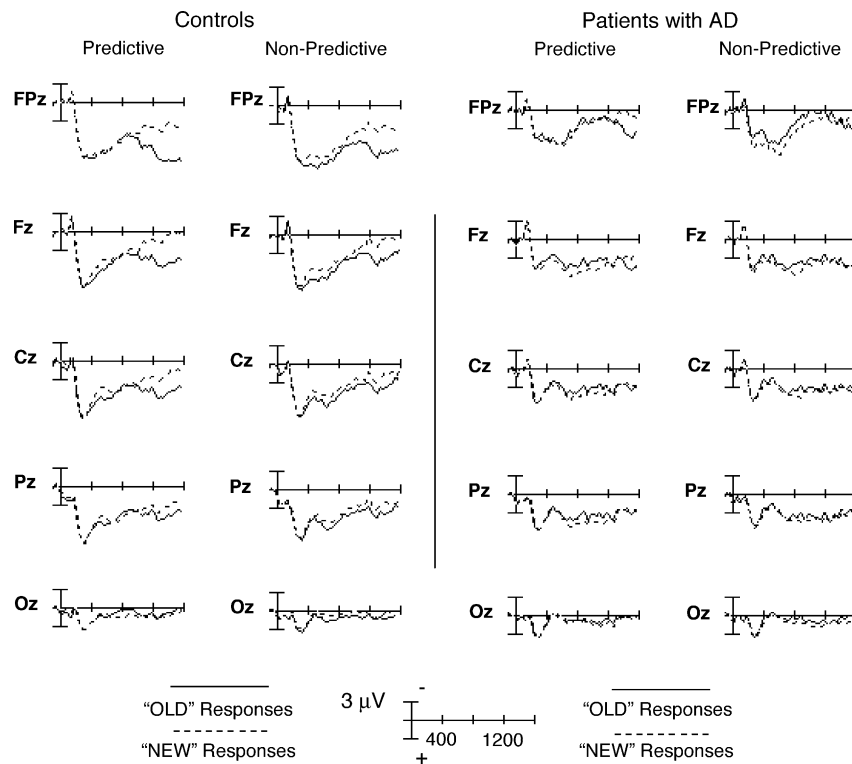


Fig. 2. Grand average ERP plots for five midline sites. ERPs of items following predictive or non-predictive contexts based on response (“Old” or “New”) for controls and patients with AD. Items following predictive and non-predictive contexts are on the left and right columns, respectively, for each group.

studied, and non-predictive–non-studied items. A context type (predictive, non-predictive) \times item type (non-studied, studied) \times site (FPz, Fz, Cz, Pz, Oz) \times group (controls, patients with AD) ANOVA revealed a main effect of group [$F(1,22) = 4.61, p = 0.043$] attributable to the N400 being of lower voltage in the patients with AD ($3.11 \mu\text{V}$) than controls ($5.72 \mu\text{V}$). There was also a context type \times site interaction [$F(4,88) = 10.24, p < 0.00001$]. To follow up on this interaction, separate ANOVAs were run at each midline site which revealed a main effect of context type [$F(1,22) = 5.29, p = 0.031$] only at the Pz site (see Fig. 1) due to the N400 being more attenuated following predictive compared to non-predictive contexts. There were no other main effects or interactions at this site, including context type \times group [$F(1,22) < 1$]. It should be noted that the lack of an effect or interaction with any factor of item type in the above ANOVA is likely attributable to the use of a shallow encoding task [see (Rugg, Allan, & Birch, 2000)], as reflected by poor discrimination even for the control subjects. It is, thus, probable that the studied items were contaminated by many unremembered words, reducing the likelihood of finding an ERP difference between studied and non-studied items.

3.2.2. Late frontal effects

To investigate the role of frontal processing on subject response (whether an item was endorsed as “Old” or “New”) in the setting of enhanced fluency, we calculated mean ERP amplitudes over the 1200–1600 ms latency at frontal sites (FPz, Fz) for predictive–“Old”, predictive–“New”, non-predictive–“Old”, and non-predictive–“New” items (see Fig. 2). A context type (predictive, non-predictive) \times response (“New”, “Old”) \times site (FPz, Fz) \times group (controls, patients with AD) ANOVA revealed a main effect of response [$F(1,22) = 8.60, p = 0.008$], due to greater positivity associated with “Old” responses relative to “New” responses. There was also a response \times context type interaction [$F(1,22) = 5.46, p = 0.029$], because the effect of response was larger for items following a predictive context than for those following a non-predictive context, similar to what was previously observed in young subjects (Wolk et al., 2004).

To further analyze the interaction of response \times context type, separate response (“New”, “Old”) \times site (FPz, Fz) \times group (controls, patients with AD) ANOVAs were performed for both context types. For items following a predictive context, this analysis revealed a main effect of response [$F(1,22) = 14.20, p = 0.001$] as “Old” responses were associated with greater frontal positivity than “New” responses. A response \times group interaction approached significance [$F(1,22) = 3.81, p = 0.064$] due to “Old” responses being somewhat more positive for the controls than the patients with AD (see Figs. 2 and 3). However, the effect of response was reliable for both groups [controls: $F(1,11) = 9.54, p = 0.010$; patients with AD: $F(1,11) = 5.76, p = 0.035$]. There was also a site \times response interaction [$F(1,22) = 4.43, p = 0.047$] attributable to a greater effect of response at FPz than Fz. The analogous ANOVA for items

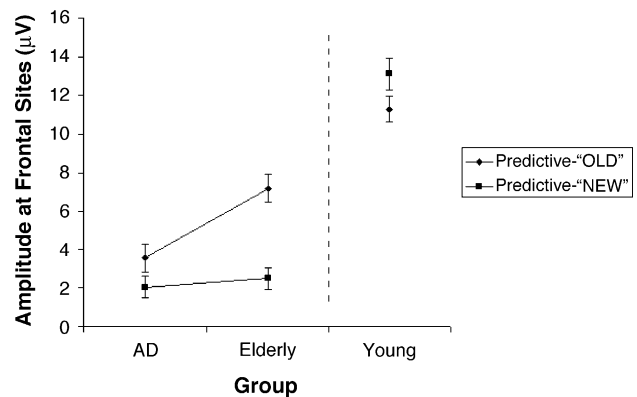


Fig. 3. ERP mean amplitude averaged over frontal sites (FPz, Fz) for the 1200–1600 ms interval for items following a predictive context based on response. The error bars reflect the S.E.M. Data for the young subjects (undergraduates) was taken from a prior study using the same paradigm (Wolk et al., 2004).

following a non-predictive context did not reveal any significant main effects or interactions. However, there was a trend towards an effect of response [$F(1,22) = 3.47, p = 0.076$] reflecting the tendency for “Old” responses to be somewhat more positive than “New” responses.

4. Discussion

In this study, we investigated the impact of conceptual fluency on the recognition judgments of patients with AD, as well as the neural correlates of this effect. The critical finding of the present contribution is that patients with mild AD—despite their poor episodic memory—appear to use conceptual fluency as a cue in recognition memory judgments. In addition, the ERP data provide further insight into the underlying neural mechanisms supporting the use of fluency in recognition judgments and the relative preservation of these processes in the setting of mild AD.

4.1. Behavioral findings

Conceptual fluency is putatively considered to impact memory by influencing the degree of familiarity invoked by an item when presented for recognition judgment (Kelly & Jacoby, 2000; Kinoshita, 1997; Rajaram & Geraci, 2000; Whittlesea & Williams, 2001a, 2001b). The capacity of patients with AD to use conceptual fluency as a cue in a recognition test is consistent with the findings from a variety of studies suggesting relative sparing of familiarity-based processing (Budson et al., 2000; Christensen et al., 1998; Dalla Barba, 1997; Gallo et al., 2004; Knight, 1998; Koivisto et al., 1998). As recollection is disproportionately impaired in AD, the degree to which an item feels familiar may then be the critical factor in recognition decisions, which appears the case in the present study.

It should be noted that patients with AD exhibited very poor memory in this study ($d' = 0.06$). Although conceptual fluency clearly dictated performance at test in this context, the present data cannot inform whether such cues are useful or valid in making recognition decisions. The degree to which conceptual fluency is enhanced by prior study determines its validity as a cue [see Verfaellie & Cermak (1999) for a similar discussion]. In the present work, the shallow nature of the encoding condition likely resulted in minimal enhancement of conceptual fluency for the studied items (reflected, perhaps, by the lack of N400 modulation associated with study status). Indeed, the context type manipulation appeared to have a greater impact on conceptual fluency than whether or not an item was on the prior study list. Thus, in this study, conceptual fluency was not a valid basis for determining prior study for the patients with AD. As such, use of these cues only produced a greater bias to categorize more fluent items (items following a predictive context) as “Old”, but did not impact discrimination. Although the poor discrimination of the patients limits comment on whether conceptual fluency cues drive veridical memory judgments, the present data demonstrated a clear influence of such cues on test performance in the setting of poor memory.

That the recognition performance of the patients with AD was so poor is not surprising given the difficulty of the task (as suggested by the poor discrimination of the controls). However, the lack of clear memory effects in the patients with AD does at least raise the possibility that they were not performing the task as a recognition memory test. In other words, their decisions may have been based on some other factor rather than whether or not they thought the items were previously studied. While the possibility that they misunderstood or forgot the test instructions cannot be excluded with certainty, several factors suggest that the patients with AD were performing the task as specified. First, these patients had mild impairment and appeared to understand the task instructions. To confirm, patients were always asked to describe in their own words the nature of the task accurately prior to proceeding with the test. Their understanding was re-assessed at a pause after the first 10 test items. Second, the “Old or New?” prompt preceding each test item should have served as a cue that the task involved a memory decision. Further, given their need to respond “Old” or “New”, it is unclear what other task would be consistent with such a response. Finally, as conceptual fluency impacts recognition memory performance in healthy young and older controls, it would seem most likely that the similar effect of fluency found in patients with AD is due to the impact of such a manipulation on memory decisions rather than the performance of an unspecified, alternative task. Thus, it appears most parsimonious to assume that their responding was a reflection of recognition memory judgments.

The finding of an inverse correlation between discrimination and the fluency effect in control subjects supports the notion that healthy subjects also use fluency cues in their recognition judgments, particularly when their memory is

poor. This relationship of poor memory and greater utilization of fluency cues is consistent with several studies examining perceptual fluency manipulations (Johnston et al., 1991; Verfaellie & Cermak, 1999; Westerman et al., 2002, 2003). For example, Verfaellie and Cermak (1999) found that control subjects were less likely to use perceptual fluency cues in their recognition judgments than patients with temporo-limbic amnesia; who, not unexpectedly, displayed poorer overall accuracy. However, when they then equated the memory performance of the two groups by use of a *counterfeit* study list, in which there can be no discrimination between studied and non-studied items, both groups utilized perceptual fluency cues to a similar extent. This result suggests that although patients with impaired memory may rely on fluency cues to a greater extent than those with normal memory, healthy subjects also rely on such cues when their memory is weak. The current study is consistent with this conclusion, and the first to demonstrate the relationship of poor memory with greater reliance on fluency in healthy subjects using a manipulation of conceptual fluency.

Patients with AD endorsed items as “Old” 9% more often when following a predictive compared to non-predictive context while this *fluency effect* was 8% for the controls; thus, despite the prediction based on the above logic that patients with AD, due to their poorer memory, would have a greater fluency effect than controls, the manipulation of conceptual fluency had a similar absolute effect on performance at test for both groups. Indeed, this result does not conform to the above-mentioned perceptual fluency study, in which the poorer discrimination of patients with amnesia was associated with a greater reliance on fluency (Verfaellie & Cermak, 1999).

Several possibilities may explain the lack of the expected larger fluency effect on the patients with AD than controls. With regard to the study by Verfaellie and Cermak (1999), deviation from their results could be due to a number of methodologic factors, including the independent variable manipulated (perceptual versus conceptual fluency). In particular, their use of a much shorter study list (40 items) and a younger control group (mean age = 50.8 years) resulted in a more accurate memory performance for their controls relative to ours. The much higher discrimination of their control subjects appeared to eliminate any use of fluency cues in their recognition judgments whereas our control subjects still relied upon such cues. Additionally, the difference in their control accuracy relative to the patients with amnesia was much greater than between our controls and patients with AD. Thus, the relatively modest memory advantage of our controls compared to the patients may have limited the sensitivity of the present study to find a group difference in the fluency effect.

Alternatively, the lack of an increased reliance on fluency for the patients with AD relative to the controls may reflect a reduced capacity or tendency to use these cues compared to healthy subjects for a given level of memory performance. This would suggest that the relationship between discrimination and fluency effect is modified by AD. Although it is

unclear from the present data why this would be the case, one speculation is that the patients with AD may be impaired in their capacity to monitor their performance. Even at early stages of AD, patients often underestimate the severity of their cognitive deficits (Derouesné et al., 1999; Ott et al., 1996). This underestimation could then result in a reduced tendency to use fluency cues at a given level of memory accuracy relative to controls. Another possibility is that the patients with mild AD may have a relative impairment in their capacity to assess and attribute conceptual fluency to prior study (see ERP results below). Further work in which memory accuracy is matched for healthy subjects and those with AD would be informative in this regard.

It is important to emphasize that despite the failure to find a greater absolute fluency effect in the patients with AD, it appears that such cues exerted a greater influence on their overall performance at test than that of the controls. For example, one way to gauge the relative impact of fluency on performance is to compare the effect of fluency (predictive versus non-predictive) with the effect of the actual status of the items (studied versus non-studied) on the rate of “Old” endorsements. Patients with AD endorsed studied items as “Old” only 2% more often than non-studied items. By this measure, the impact of fluency on responding was 4 1/2 times greater (9%/2%) than whether or not an item was actually studied. As controls were 14% more likely to endorse a studied item as “Old” relative to a non-studied one, fluency had a proportionally smaller impact on the controls (8%/14%). This finding suggests that fluency may play an important role in the mnemonic experience of patients with mild AD.

One other noteworthy aspect of the behavioral data is that the effect of conceptual fluency had an equivalent impact on the proportion of “Old” endorsements for both studied and non-studied items. Arguing from a dual-process model in which fluency selectively influences familiarity, one would predict a greater effect on non-studied than studied items. This expectation is due to the fact that the conceptual fluency manipulation should only impact those studied items in which there is no recollection whereas this is the case for all of the non-studied items. Of course, this result is not surprising for the patients with AD given their very poor discrimination. Studied and non-studied items had essentially the same mnemonic content, resulting in enhanced conceptual fluency having a similar effect on both item types.

Although this logic may apply less so to the controls, it again must be noted that given the shallow nature of the study task and lengthy number of items, their discrimination was also poor and likely largely driven by familiarity. The familiarity of both studied and non-studied items then should have been enhanced to a similar degree with the manipulation of context type, resulting in a similar impact on recognition judgments regardless of study status. This explanation is consistent with work by Rajaram and Geraci (2000) also using a manipulation of conceptual fluency. The discrimination of the participants in that study was much higher than the controls of the current study. They found a reduced effect of

fluency on “Old” endorsements of studied relative to non-studied items. However, using the remember/know procedure as an estimate of recollection and familiarity (Gardiner, 1988), familiarity was equally influenced by the fluency manipulation regardless of study status whereas recollection was unaffected [for a similar result in a perceptual fluency paradigm see (Rajaram, 1993)]. It should be noted that other conceptual fluency studies have found equivalent effects on “Old” endorsements of studied and non-studied items even in the setting of relatively high discrimination (Whittlesea, 1993; Whittlesea & Williams, 2001a). Unfortunately, these studies did use process estimation methods to compare to the findings of Rajaram and Geraci (2000).

A final point about the behavioral data; although the present results can be accounted for under the assumptions of a dual-process model, the data also appear consistent with a single-process account of recognition memory, in which fluency results in either greater apparent “memory” strength or a greater bias to classify an item as “Old”. In fact, it could be argued that even if a dual-process account is accepted, the poor recollection of the healthy controls and patients with AD creates a mnemonic state that is effectually governed by a single process. Thus, the present data cannot adjudicate between these models.

4.2. *Electrophysiological results*

Consistent with the behavioral results, patients with AD demonstrated a relative preservation of the ERP modulations (N400 and late frontal) seen in the control subjects, providing support beyond the behavioral data for the integrity of the neural mechanisms underlying the use of fluency cues. With respect to the experimental conditions producing these modulations, the current results are also qualitatively similar to our prior work in undergraduate subjects (Wolk et al., 2004).

Items following a predictive context were found to be associated with an attenuated N400 at Pz compared to when following a non-predictive context. This result argues that the semantic network of the patients with mild AD was preserved relative to that of the controls, at least with regards to sensitivity to semantic context produced by the sentence stem manipulation. As N400 modulation may be related to the ease with which an item is semantically integrated into its context (Holcomb, 1993; Misra & Holcomb, 2003; Rugg & Doyle, 1994), its attenuation suggests more fluent conceptual processing for items following a predictive sentence context. That the degree of this attenuation did not differ between the two groups, suggests, along with the behavioral data, that the experimental manipulation modulated fluency to a similar extent in both groups. This result is important because other studies have found mixed results on the impact of semantic priming on facilitated processing as measured by the N400 in patients with AD (Auchterlonie, Phillips, & Chertkow, 2002; Ford et al., 2001, 1996; Hamberger, Friedman, Ritter, & Rosen, 1995; Iragui, Kutas, & Salmon, 1996; Revonsuo, Portin, Juottonen, & Rinne, 1998; Schwartz,

Federmeier, Van Petten, Salmon, & Kutas, 2003). Although a lack of group difference must be interpreted with caution, the effect size of the interaction was quite small ($\eta^2 = 0.01$), explaining only a tiny fraction of the variance of the results. This small effect size suggests that our not finding a group difference in the N400 modulation of fluency is not related to the relatively small numbers of subjects in the present study.

As discussed above, processing involved in attribution of enhanced fluency to prior study versus alternative sources is critical to whether enhanced fluency impacts recognition judgments. Based on our work with undergraduate subjects, we proposed that late frontally maximal activity may reflect this attributional processing (Wolk et al., 2004). Consistent with this result, both groups in the present study exhibited greater frontal modulation (1200–1600 ms) associated with response (“Old” or “New”) in the setting of enhanced fluency (items following a predictive context) than when fluency was not enhanced (items following a non-predictive context). This result provides additional support for the critical role of such frontal activity in making recognition judgments, or attributions, in the setting of enhanced fluency. Post-retrieval processes (such as source monitoring) occur in a similar frontal distribution and latency (Goldmann et al., 2003; Nessler et al., 2001; Ranganath & Paller, 2000; Wilding et al., 1995; Wilding & Rugg, 1996, 1997a, 1997b). The attributional activity may then be considered a form of post-retrieval processing if fluency cues created from prior study, as opposed to from direct experimental manipulation as in the current study, undergo attributional processing.

Although one should be cautious in assuming the location of neural generators based on surface recordings, the finding of relative sparing of frontally distributed activity in the patients with AD is noteworthy given other work demonstrating impairments of processing dependent on frontal lobe activity (Amieva, Phillips, Della Sala, & Henry, 2004; Baddeley, Baddeley, Bucks, & Wilcock, 2001; Baddeley, Bressi, Della Sala, Logie, & Spinnler, 1991; Dalla Barba, Nedjam, & Dubois, 1999), even early in the course of AD (Perry, Watson, & Hodges, 2000). This dysfunction is manifested by impairments of response inhibition, attentional switching, divided attention, and working memory. Prefrontal activity is also thought to underlie post-retrieval processing, particularly in the dorsolateral prefrontal cortex (see Fletcher & Henson, 2001), and its dysfunction has been hypothesized to be responsible for the impairments of source monitoring (Dalla Barba et al., 1999) and other post-retrieval processing activity (Budson et al., 2002) seen in patients with AD. The current result represents a possible prefrontally mediated attributional process that is relatively spared in mild AD. Inasmuch as conceptual fluency contributes to veridical memory outside the laboratory, this spared processing may play a critical role in the accurate memory judgments of patients with AD. However, there was a trend for this activity to be blunted compared to control subjects, perhaps reflecting early, mild dysfunction in fluency related attributional processing. Study of patients with AD further progressed in the disease course

would provide additional insight into how long such processing is relatively preserved.

Finally, it is worth noting that although the data demonstrate that aging and mild AD do not eliminate response-related frontal activity in the setting of enhanced fluency, this activity is of lower voltage and reversed polarity from our prior work in young subjects (see Fig. 3). This result suggests that aging alters the way fluency is handled at the neural level. The reason for this difference is unclear and merits further investigation.

5. Conclusions

The present work demonstrates two major findings. First, patients with mild AD appear capable of using conceptual fluency cues as a basis for making judgments on a recognition memory task. The potential importance of such cues is highlighted by the finding that the manipulation of fluency had a larger impact on responding than whether or not an item was *actually* studied. Second, the electrophysiological activity underlying the use of fluency in recognition memory was relatively intact in mild AD. As other frontally based processes are impaired in this population, it is particularly notable that the late frontal activity associated with attributional processing is relatively preserved.

The capacity of patients with mild AD to use fluency cues in a recognition memory task and their dependence on familiarity-based processing suggest that conceptual fluency cues may be critical for these patients' everyday memory outside of the laboratory. Techniques to maximally utilize fluency cues may actually improve recognition accuracy, as suggested in patients with amnesia (Dorfman, Kihlstrom, Cork, & Misiaszek, 1995; Verfaellie, Giovanello, & Keane, 2001). However, when fluency is not related to prior study (as in the present investigation), use of such cues may actually contribute to false recognition without aiding discrimination. Future studies will further test the hypothesis that fluency is critically important for understanding the true and false memories of patients with AD.

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