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Comparison of the serial position effect in very mild Alzheimer's disease, mild Alzheimer's disease, and amnesia associated with electroconvulsive therapy

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Abstract

Individuals given a series of words to memorize normally show better immediate recall for items from the beginning and end of the list than for midlist items. This phenomenon, known as the serial position effect, is thought to reflect the concurrent contributions of secondary and primary memory, respectively, to recall performance. The present study compared the serial position effects produced on Trial 1 of the California Verbal Learning Test (CVLT) in mildly demented ($N = 25$; M MMSE $= 20.0$) and very mildly demented ($N = 25$; M MMSE $= 25.5$) patients with Alzheimer's disease (AD), and age- and education-matched normal control (NC) participants ($N = 50$). In addition, the serial position effects of the very mildly demented AD patients were compared to those of patients with a transient, circumscribed amnesia arising from a prescribed series of electroconvulsive therapy (ECT) treatments for the relief of depressive illness ($N = 11$). While the NC group exhibited the typical serial position effect, AD patients recalled significantly fewer words than NC participants overall, and exhibited a significantly reduced primacy effect (i.e., recall of the first 2 list items) with a normal recency effect (i.e., recall of the last 2 list items). Patients with circumscribed amnesia due to ECT were as impaired as the very mildly demented AD patients on most standard CVLT measures of learning and memory, but exhibited primacy and recency effects, which were within normal limits. These results suggest that a reduction in the primacy effect, but not the recency effect, is an early and ubiquitous feature of the memory impairment of AD. It is not, however, a necessary feature of all causes of memory impairment. (*JINS*, 2000, *6*, 290–298.)

Keywords: Alzheimer's disease, CVLT, ECT, Serial position effects

INTRODUCTION

It is well known that when individuals are given a list of items to memorize, they normally show better recall for items from the beginning (i.e., primacy effect) and end (i.e., recency effect) of the list than for those from the middle portion (Glanzer, 1972; Glanzer & Cunitz, 1966). Thus, if the probability of recall is plotted against the list position of each item, a *U*-shaped serial position curve is obtained (Murdock, 1962). One widely accepted interpretation of this serial position effect is that it reflects the operation of two independent memory systems: primary (or short-term) memory, which is a time-dependent, limited-capacity store that allows the most recent items to be better recalled than other items, and secondary (or long-term) memory, which is an actively accessed, long-lasting store that allows early list items that received the greatest amount of rehearsal to be better recalled than other items.

Some of the strongest evidence supporting this two-memory system model of the serial position effect comes from the study of patients with relatively localized brain damage that appears to differentially affect one or the other system. Patients with amnesia due to damage to medial temporal lobe or diencephalic brain structures, for example, have been characterized as having a deficit in secondary memory with relatively preserved primary memory and studies have consistently shown that they exhibit an abnormally small primacy effect coupled with a preserved recency effect (Baddeley & Warrington, 1970; Carlesimo et al.,1996; Her-

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mann et al., 1996). Several studies of patients with temporoparietal cortex damage following stroke or head injury, in contrast, have shown that these patients may have a short-term retention (i.e., primary memory) deficit with relatively intact secondary memory and that they exhibit normal primacy and impaired recency effects on tests of free recall (Basso et al., 1982; Vallar & Papagano, 1986; Warrington et al., 1971; Warrington & Shallice, 1969).

The anomalous serial position curves exhibited by patients with localized brain damage have also been observed in demented patients with probable Alzheimer's disease (AD). Alzheimer's disease is a progressive neurodegenerative disorder that results in neuron loss, synapse loss, and the presence of characteristic pathologic lesions (i.e., neurofibrillary tangles, neuritic plaques) primarily in the medial temporal lobe brain structures (e.g., hippocampus, entorhinal cortex, parahippocampal gyrus) and the association cortices of the temporal, parietal, and frontal lobes (Terry & Katzman, 1983; Terry et al., 1981, 1991). Like patients with amnesia, AD patients have a prominent secondary memory deficit, most likely due to the involvement of medial temporal lobe structures, and studies have consistently shown a reduced primacy effect that is evident even in the relatively early stages of the disease (Capitani et al., 1992; Carlesimo et al., 1995; Greene et al., 1996; Massman et al., 1993; Miller, 1971; Pepin & Eslinger, 1989; Spinnler et al., 1988). Primary memory, in contrast, is often preserved in the early stages of AD and several studies have demonstrated a normal recency effect in mildly demented AD patients (Massman et al., 1993; Pepin & Eslinger, 1989; Simon et al., 1994). However, as the disease progresses and other cortical and subcortical brain regions become involved, a reduction in primary memory and the recency effect may become evident as well (Kesner et al., 1989; Pepin & Eslinger, 1989).

While this general progression of change in the serial position effect in patients with AD is supported by several studies that cross-sectionally compared mildly and moderately demented patients (Kesner et al., 1989; Pepin & Eslinger, 1989), little is known about the nature of the serial position effect in very mildly demented patients who are in the earliest stages of the disease. A number of recent studies have shown that a deficit in secondary memory is among the earliest manifestations of AD and may often precede the development of the full dementia syndrome (Bondi et al., 1994; Fuld et al., 1990; Grober & Kawas, 1997; Linn et al., 1995; Masur et al., 1994). These findings suggest that a reduced primacy effect may characterize free recall performance from the earliest stages of the disease. It may be the case, however, that the primacy effect is not reduced very early in the course of AD, when the secondary memory deficit is relatively mild, and is only affected when secondary memory becomes more impaired later in the disease. To address this issue, the present study compared the serial position effect in very mildly demented and mildly demented patients with AD by examining their performances on the initial trial of a rigorous list learning task, the California Verbal Learning Test (CVLT).

Furthermore, to determine if any change in the serial position effect in very mildly demented patients with AD was specific to a global dementing disorder or a general characteristic of mild secondary memory deficit due to any cause, the AD patients' performance was compared to that of patients with an equally severe, but relatively circumscribed and time-limited amnesia arising from a prescribed series of electroconvulsive therapy (ECT) treatments for the relief of depressive illness. It is well known that memory impairment is a prominent side-effect of ECT (Cahill & Frith, 1995; Squire, 1986) and that the amnesia produced in this manner is at its most severe immediately following treatment and then gradually dissipates over time. Although the specific cause of the amnesia associated with ECT is not known, some investigators have suggested that it may be due to the temporary disruption of the medial temporal lobe structures that are thought to mediate secondary memory (Inglis, 1970; Squire, 1984; Squire et al., 1984). By comparing the serial position effect in very mildly demented AD patients and patients with amnesia due to ECT who have similarly mild secondary memory deficits, the influence of any additional cognitive deficits associated with AD on the nature of the effect could be examined.

METHODS

Research Participants

Fifty patients with the diagnosis of probable ($N = 40$) or possible ($N = 10$) dementia of the Alzheimer type (30 women and 20 men) and 50 neurologically intact normal controls (NC) (24 women and 26 men) took part in the present study. Eleven participants (all men) who were receiving electroconvulsive therapy (ECT) for the treatment of major depression also participated in the present study. All AD and NC participants were participants in an ongoing longitudinal study at the University of California, San Diego (UCSD) Alzheimer's Disease Research Center (ADRC) through which they received annual physical, neurological, and neuropsychological evaluations. On the basis of these evaluations and a number of laboratory tests used to rule out other causes of dementia (e.g., hypothyroidism, vitamin B12 deficiency, electrolyte imbalance), the diagnosis of probable or possible AD was made by two senior staff neurologists at the ADRC according to the criteria developed by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA; McKhann et al., 1984). To reduce the possibility of including individuals with multi-infarct dementia, patients with a score of 5 or greater on the Rosen-modified Hachinski ischemia scale (Hachinski et al., 1975; Rosen et al., 1980) were excluded from the AD patient group. The exclusion criteria for the NC group also included a history of severe head injury, alcoholism, or serious psychiatric disturbance. It should be noted that the diagnosing neurologists were only provided

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with a general statement concerning the results of the neuropsychological evaluation (e.g., a deficit in two or more areas of cognition), but were not aware of any specific test scores.

The mean age, years of education, and scores on the Mini-Mental State Examination (MMSE; Folstein et al., 1975) and the Dementia Rating Scale (DRS; Mattis, 1976) of the AD and NC participants are shown in Table 1. An alpha level of .05 was used for all statistical tests. The patients with AD and the NC participants did not differ significantly in mean age [$t(98) = -0.16$, $p = .88$] or mean years of education [$t(98) = -0.4$, $p = .69$], but the AD patients scored significantly lower than the NC group on the DRS [$t(98) = 12.52$, $p < .0005$] and MMSE [$t(98) = 12.46$, $p < .0005$].

To examine the influence of dementia severity on the serial position effect, the AD patient group was divided into *very mild* ($N = 25$) and *mild* ($N = 25$) groups on the basis of MMSE scores. Patients scoring above the median MMSE score of 23.5 were considered very mildly impaired, and those scoring below the median were considered mildly impaired. Only 5 of the 25 mild AD patients scored below 18, the MMSE cut-off score for mild dementia suggested by Tombaugh and McIntyre (1992). The mean age, years of education, MMSE scores, and DRS scores of the mild and very mild AD subgroups are also presented in Table 1.

A series of one-way analyses of variance (ANOVA) comparing the mild AD, very mild AD, and NC participants revealed no significant differences in age [$F(2,97) = 0.08$, $p = 0.91$] or years of education [$F(2,97) = 0.39$, $p = .68$]. The groups did differ significantly, however, in mean MMSE [$F(2,97) = 255.7$, $p < .00005$] and DRS [$F(2,97) = 146.6$, $p < .00005$] scores. *Post-hoc* comparisons with Newman-Keuls tests revealed that the mild AD and very mild AD groups had lower mean scores than the NC participants on both tests ($p < .05$), and that the mild AD group scored lower on both tests than the very mild AD group ($p < .05$).

It should be noted that 1 participant from the very mild AD group and 1 from the mild AD group had participated in a previously reported study (Massman et al., 1993), which also examined serial position effects in the CVLT performance of AD patients. However, the study by Massman and colleagues did not examine the influence of dementia severity on the serial position effect.

The patients who received ECT had a mean age of 52.6 ($SD = 13.5$) years and a mean of 14.8 ($SD = 2.3$) years of education. The ECT patients were significantly younger than the NC, very mild AD, and mild AD participants [$F(3,110) = 27.6$, $p < .00005$; Newman-Keuls *post-hoc* comparisons, $p < .05$], but the groups did not significantly differ in years of education [$F(3,110) = 0.34$, $p = .79$]. The mean MMSE score of the ECT group (25.5; $SD = 2.50$) did not differ significantly from that of the very mild AD patients, but was significantly below that of the NC group [$F(3,110) = 153.3$, $p < .00005$; Newman-Keuls *post-hoc* comparisons $p < .05$]. The MMSE scores of the ECT group were not within the normal range due mainly to poor performance on the memory items of the test. Eight participants received bilateral ECT and the remaining 3 received either unilateral ECT to the nondominant hemisphere (2 participants) or a combination of unilateral and bilateral treatments (1 participant).

Neuropsychological Tests

The MMSE was administered according to the procedures of Folstein et al. (1975), and the DRS was administered according to the procedures of Mattis (1976), with the exception that all items were administered to all participants. The DRS yielded five subscores for the cognitive capacities of *attention*, *initiation and perseveration*, *construction*, *conceptualization*, and *memory*.

The California Verbal Learning Test (CVLT; Delis et al., 1987a) is a standardized test of verbal learning and memory which involves the oral presentation of a list of 16 "shopping items" (List A) from four categories (*fruits*, *spices or herbs*, *clothing*, and *tools*). The words are presented in the same order for five trials. After each trial, participants are asked to recall as many items as possible in any order, including those reported on previous trials. Following the five trials, a second list (List B) is presented once, which contains 16 new items from two of the same categories as List A

Table 1. Age, education, Mini-Mental State Examination (MMSE) and Dementia Rating Scale (DRS) scores for patients with Alzheimer's disease (AD) and normal control (NC) participants

	Group				AD subgroups			
	NC ($N = 50$)		AD ($N = 50$)		Very mild ($N = 25$)		Mild ($N = 25$)	
Variable	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)
Age (years)	73.7	(6.1)	73.8	(6.4)	73.5	(6.6)	74.2	(6.4)
Education (years)	14.2	(3.4)	14.5	(3.1)	14.8	(3.3)	14.2	(3.0)
MMSE	29.2	(1.0)	22.7*	(3.5)	25.5*	(1.6)	19.9*#	(2.6)
DRS	138.3	(4.4)	118.8*	(10.0)	125.3*	(6.7)	112.4*#	(8.7)

*Significant difference *vs.* NC, $p < .05$.
#Significant difference between very mild AD and mild AD, $p < .05$.

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(*fruits* and *spices or herbs*) and two new categories (*kinds of fish* and *kitchen utensils*). Participants are asked to recall as many items from List B as possible. Immediately following List B, free and category-cued recall of List A is elicited. After a 20-min delay that is filled with unrelated nonverbal testing, free recall, category-cued recall, and recognition of List A items are assessed.

Procedure

The CVLT, the MMSE, and the DRS were administered to all AD patients and NC participants as part of a larger battery of neuropsychological tests (see Salmon & Butters, 1992). The tests were administered on the same day within the same test session. None of the participants had been previously tested with the CVLT, but some had been given the MMSE and DRS during previous annual evaluations. The participants were individually tested by a trained psychometrist in a quiet, well-lit room.

Neuropsychological tests were administered to the patients both prior to ECT treatment and approximately 3 to 7 hours following the last of a series of treatments (range of treatments = 5–11, $M = 7.4$). The pre-ECT and ECT tests were separated by an average of 20.8 days (range 13–35). In order to reduce interference between test sessions, alternate forms of the CVLT (Form I: Delis et al., 1987a; and Form II: Delis et al., 1987b) were used on the 2 test days. The order of administration of alternate forms was counterbalanced across participants. Only data obtained on the day of ECT are reported here, and are derived from Form I for 5 participants and from Form II for 6 participants.

RESULTS

Overall California Verbal Learning Test Performance

The mean scores achieved by the NC participants, the entire AD patient group, the very mild AD and mild AD subgroups, and the ECT patient group on a number of key CVLT measures are shown in Table 2. The overall AD patient group scored significantly lower than the NC group on Trial 1 Recall [$t(98) = 8.47, p < .001$], Trial 5 Recall [$t(98) = 14.41, p < .001$], learning over Trials 1 to 5 [$t(98) = 13.5, p < .001$], Short-Delay Free Recall [$t(98) = 13.25, p < .001$], Long-Delay Free Recall [$t(98) = 14.96, p < .001$], and on a Discriminability measure that quantifies the ability to discriminate target words from distracters on the Delayed Recognition Test [$t(98) = 13.3, p < .001$].

When the AD patient group was divided into very mild and mild subgroups, both patient groups performed significantly worse than the NC group on all of these key CVLT measures (all ps $< .05$). In addition, the mild AD group performed worse than the very mild AD group on Trial 5, Trials 1 to 5 and Discriminability (all ps $< .05$).

The CVLT performance of the ECT group was directly compared to that of the very mild AD group. There were no significant differences between groups on Trial 1 Recall [$t(34) = 0.27, p = .79$], Trial 5 [$t(34) = -0.16, p = .87$], learning over Trials 1 to 5 [$t(34) = -0.57, p = .57$], Short-Delay Free Recall [$t(34) = 0.45, p = .66$], or Long-Delay Free Recall [$t(34) = 0.20, p = .84$]. The ECT group scored significantly higher than the very mild AD group on the Discriminability measure [$t(34) = -2.02, p = .05$].

Serial Position Effects

Overall AD versus *NC*

Figure 1 presents the proportion of AD patients and NC participants who recalled each item on the first recall trial of the CVLT as a function of the serial position of the item. As the figure shows, the classic *U*-shaped serial position curve was obtained for the NC group. In contrast, AD patients did not exhibit a pronounced *U*-shaped function, primarily due to an attenuation of the primacy portion of the curve. On the basis of the serial position curve obtained for the NC group, primacy and recency effects were defined as the re-

Table 2. Raw scores achieved by normal control (NC) participants, patients with Alzheimer's disease (AD), and patients who received electroconvulsive therapy (ECT) on key measures of the California Verbal Learning Test (CVLT)

	Group									
	NC		AD		Very mild AD		Mild AD		ECT	
Score	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)
Trial 1	6.4	(2.2)	3.4*	(1.3)	3.7*	(1.4)	3.0*	(1.2)	3.5	(1.2)
Trial 5	11.7	(2.6)	5.3*	(1.8)	6.2*	(1.9)	4.4*#	(1.3)	6.3	(2.0)
Trials 1–5	48.3	(10.0)	22.9*	(7.5)	25.8*	(6.9)	20.0*#	(7.0)	27.4	(8.4)
Short-Delay Free Recall	9.2	(3.5)	1.5*	(2.1)	1.8*	(2.4)	1.3*	(1.7)	1.5	(1.0)
Long-Delay Free Recall	9.8	(3.5)	1.2*	(2.0)	1.8*	(2.4)	0.6*	(1.4)	1.6	(2.0)
Discriminability (%)	92.3	(6.10)	67.7*	(11.6)	71.5*	(12.3)	63.9*#	(9.70)	80.0‡	(9.92)

*Significant difference *vs.* NC, $p < .05$.
#Significant difference between very mild AD and mild AD, $p < .05$.
‡Significant difference between very mild AD and ECT, $p < .05$.

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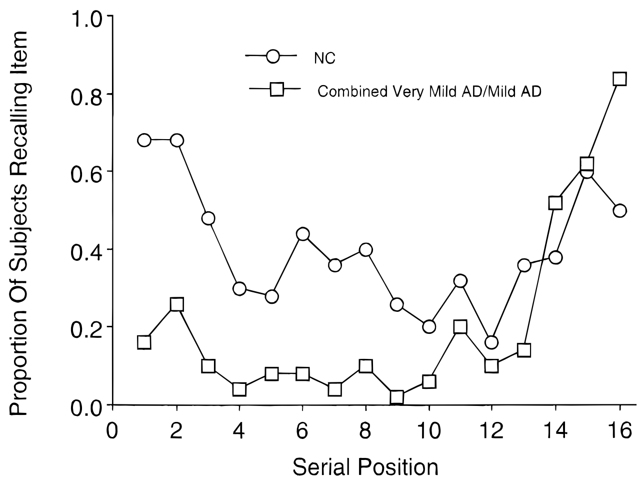

Fig. 1. The proportion of Alzheimer's disease (AD) patients and normal controls (NC) who recalled each item on the first recall trial of the CVLT as a function of the serial position of the item.

call of Items 1 and 2 and Items 15 and 16, respectively. In order to demonstrate that primacy and recency recall corresponded to this definition, the proportion of participants within each group who recalled items from the primacy, middle (Items 3–14) and recency portions of the curve were compared. The Wilcoxon matched-pairs signed-rank test was used and was followed by the Holm adjustment to correct for multiple comparisons (Holm, 1979). For the NC group, middle item recall was significantly reduced compared to primacy ($p < .0001$) and recency ($p = .002$) recall. However, no significant difference was found between primacy and recency recall ($p = .30$). For AD patients, primacy and middle item recall were not significantly different ($p = .12$). However, recency recall was found to be significantly greater than primacy ($p < .0001$) or middle item recall ($p < .0001$).

A between-groups comparison revealed that a greater proportion of NC participants than AD patients recalled one or more of the two primacy items on Trial 1 [$\chi^2(1, N = 100) = 31.3$, $p < .001$], whereas similar proportions of the AD patients and NC participants recalled one or more of the two recency items [$\chi^2(1, N = 100) = 2.70$, $p = .41$].

Very mild AD versus *mild AD*

The proportion of mild AD and very mild AD patients who recalled each item on the first recall trial of the CVLT are shown as a function of the serial position of the item in Figure 2. The serial position curve of the NC participants is also shown for comparison purposes. Both AD patient groups showed similar attenuation of the primacy portion of the serial position curve. The proportion of subjects recalling items from the primacy, middle (Items 3–14) and recency portions of the curve were compared using the Wilcoxon matched-pairs signed-rank test followed by the Holm adjustment to correct for multiple comparisons (Holm, 1979) as described above. Both very mild and mild AD groups showed a similar pattern of results. Primacy item recall was not significantly different from middle items recall in either the very mild AD ($p = .13$) or mild AD ($p = .60$) groups. However, recency recall in the very mild AD group was found to be significantly greater than primacy ($p = .003$) or middle item ($p < .00001$) recall. Likewise, recency recall in the mild AD group was found to be significantly greater than primacy ($p < .00001$) or middle item ($p < .00001$) recall.

A comparison of the performances of the two AD patient groups and the NC participants revealed an overall significant difference in the proportion of participants who recalled one or more items from the primacy portion of the list [$\chi^2(2, N = 100) = 32.6$, $p < .001$]. *Post-hoc* comparisons with Fisher's Exact Test followed by the Holm adjustment to correct for multiple comparisons (Holm, 1979), demonstrated that while smaller proportions of very mild ($p < .001$) and mild ($p < .001$) AD patients recalled primacy items compared to NC participants, similar proportions of the two AD subgroups recalled one or more primacy items ($p = .72$). There was no significant difference in the proportion of very mild AD, mild AD, or NC participants who recalled one or more recency items [$\chi^2(2, N = 100) = 2.83$, $p = .24$].

ECT versus *NC and very mild AD*

Figure 3 presents the proportion of ECT patients who recalled each item on the first recall trial of the CVLT as a function of the items' serial position. The serial position curves of the NC participants and very mild AD patients are also shown for comparison purposes. As for the NC group, a classic *U*-shaped serial position curve was obtained for the ECT patients. The proportion of participants recalling items from the primacy, middle (Items 3–14), and recency portions of the curve were compared using the Wilcoxon matched-pairs signed-rank test followed by the Holm ad-

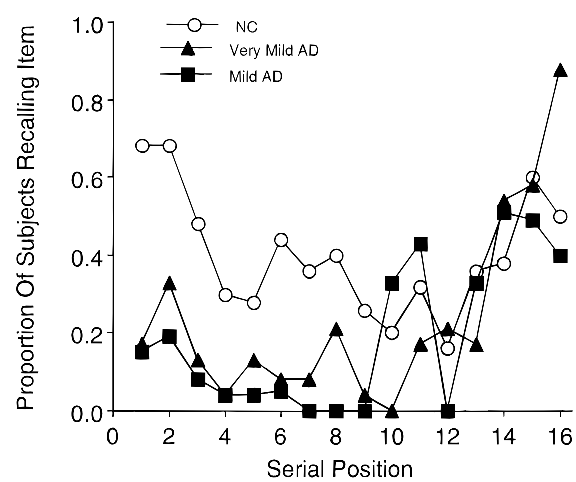

Fig. 2. The proportion of mild Alzheimer's disease (AD), very mild AD patients and normal controls (NC) who recalled each item on the first recall trial of the CVLT as a function of the serial position of the item.

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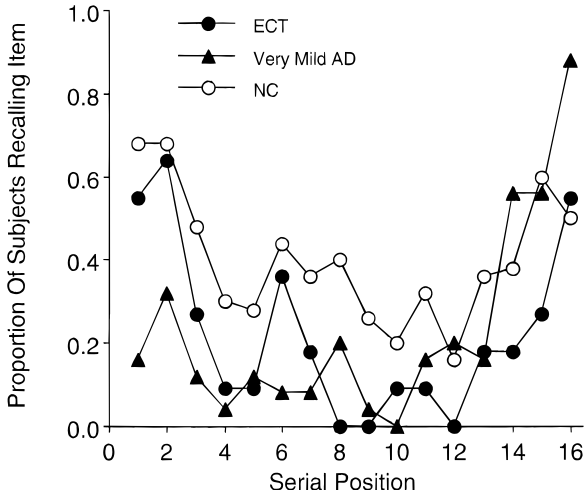

Fig. 3. The proportion of electroconvulsive therapy (ECT) patients who recalled each item on the first recall trial of the CVLT as a function of items' serial position. The serial position curves of the normal controls (NC) and very mild Alzheimer's disease (AD) patients are shown for comparison.

justment to correct for multiple comparisons (Holm, 1979), as described above. Results showed that the serial position curve of the ECT group was similar in form to that of the NC group as middle item recall was significantly reduced compared to primacy ($p = .02$) and recency ($p = .03$) recall while primacy and recency recall did not differ significantly ($p = .29$) from each other. In order to demonstrate that the ECT results were not primarily dependent upon the laterality of ECT administration, the 3 participants who were given unilateral ECT were excluded from the results. This manipulation did not significantly change the serial position effect, and therefore the 3 unilateral participants were retained.

A comparison of the NC, very mild AD and ECT groups' performances demonstrated a significant difference in the proportions of participants who recalled one or more of the primacy items on Trial 1 [$\chi^2(2, N = 86) = 21.2, p < .0001$]. Between-group comparisons with Fisher's Exact Test followed by the Holm adjustment to correct for multiple comparisons (Holm, 1979) revealed that a smaller proportion of very mild AD patients than ECT patients recalled one or more items from the primacy portion of the list ($p < .02$), whereas there was no significant difference in the proportion of ECT patients and NC participants who recalled one or more primacy items ($p = 1.0$). The three groups did not significantly differ in the proportion of participants who recalled one or more recency items [$\chi^2(2, N = 86) = 2.78$, $p = .25$).

DISCUSSION

The results of the present study are consistent with those from previous studies (Massman et al., 1993; Pepin & Eslinger, 1989; Simon et al., 1994) in demonstrating a reduced primacy effect and a normal recency effect in the verbal free recall performance of mildly demented patients with AD. In addition, the results extend these findings to very mildly demented AD patients. Despite a less severe general memory impairment than the mildly demented AD patients and a normal recency effect the very mildly demented patients demonstrated a reduction in the primacy effect that was equal to that of the mildly demented group. These findings are compatible with the notion that very early AD is characterized by a prominent secondary memory deficit with relatively spared primary memory (Kaszniak et al., 1986; Wilson et al.,1983).

An interpretation of the reduction in the primacy effect in very mildly demented AD patients as a manifestation of an early secondary memory deficit is supported by previous studies that have shown that memory impairment is often the earliest cognitive deficit that occurs in AD (Bayles et al., 1989; Delis et al., 1991; Eslinger et al., 1985; Huff et al., 1987; Storandt et al., 1984; Welsh et al., 1991). Welsh et al. (1991), for example, demonstrated that measures of verbal learning and retention were more effective than measures of confrontation naming, verbal fluency, or praxis in differentiating mildly demented AD patients with MMSE scores above 24 from nondemented elderly individuals. More recently, studies have demonstrated that measures of verbal learning and retention, but not measures of other cognitive abilities, are significantly lower in nondemented individuals who are in the preclinical stages of AD (and subsequently manifest the typical dementia syndrome) than in those who are not (Bondi et al., 1999; Grober & Kawas, 1997; Linn et al., 1995; Masur et al., 1994). Notably, simple measures of attention and primary memory do not appear to be strongly affected early in the course of AD which may account for the normal recency effect observed in both the very mildly and mildly demented AD patient groups.

The prominence of secondary memory impairment early in the course of AD, and the decreased primacy effect that was observed in very mildly demented AD patients in the present study, is not surprising given that the initial pathology in AD occurs in the medial temporal lobe structures that are thought to mediate episodic memory. Although the temporal progression of AD pathology is not fully known, several studies suggest that the entorhinal cortex, hippocampus, and the hippocampal gyrus are all affected very early in the course of the disease and that neocortical association areas become involved later as the disease progresses (Arnold et al., 1994; Braak & Braak, 1995, 1996; Gomez-Isla et al., 1996). Damage to these medial temporal lobe structures has been shown to significantly impair secondary memory in humans (Milner, 1974; Rempel-Clower et al., 1996; Scoville & Milner, 1957; Zola-Morgan et al., 1986) and nonhuman primates (Gaffan, 1996; Squire & Zola, 1996) and to adversely affect the serial position effect in verbal list-learning tasks. Patients with circumscribed amnesia arising from anterior temporal lobe lesions, for example, show the same reduction in the primacy effect, in conjunction with a normal recency effect, that was exhibited by the AD pa-

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tients in the present study (Baddeley & Warrington, 1970; Carlesimo et al., 1996; Hermann et al., 1996).

The abnormal serial position curve produced by the very mildly demented AD patients stands in contrast to the normal *U*-shaped curve produced by amnesic ECT patients. The normal primacy and recency effects exhibited by the ECT patients occurred despite an overall reduction in verbal recall on Trial 1 of the CVLT that was comparable to that of the very mildly demented AD patients. In addition, the ECT patients were just as impaired as the very mild AD group on key CVLT measures of Trial 5 recall, learning across Trials 1 to 5, and short- and long-delay free recall. It may be the case, however, that the memory impairment of the ECT patients was not as severe as that of the very mildly demented AD patients, given that they performed significantly better than the very mild AD patients on the discriminability (i.e., recognition memory) measure from the test. Such a difference in severity of the memory impairment could account for the different serial position effects exhibited by the two groups.

The different patterns of performance across recall and recognition measures from the CVLT that were produced by the ECT and very mild AD patients also suggests that the processes underlying the memory deficits of the two groups may differ. The pattern of poor recall and recognition exhibited by the AD patients may be indicative of a primary encoding or consolidation deficit, whereas the pattern of poor recall with less severely impaired recognition exhibited by the ECT patients suggests that a deficit in retrieval may contribute to their poor memory performance. While a disruption of medial temporal lobe structures may play an important role in the amnesia induced by ECT (Squire, 1986), it is also possible that the memory deficit is exacerbated by frontal and temporal neocortical disruption. Such neocortical involvement, particularly in frontal regions, may contribute to retrieval deficiencies in ECT patients and produce a memory impairment that appears to be equivalent to that of the very mildly demented AD patients (even though their secondary memory is actually less affected). In support of this hypothesis, it has been reported that direct frontal-lobe neocortical disruption has little effect on the serial position effect, at least on an initial verbal learning trial (Eslinger & Grattan, 1994). This is possibly because primacy is mediated by verbal rehearsal mechanisms that are so automatic that they operate effectively despite frontal-lobe damage. Hence, it is possible that ECT patients showed a normal serial position effect, despite frontal-lobe disruption.

An alternative explanation for the present results is that ECT and very mild AD patients may have equivalent secondary memory deficits due to dysfunction of medial temporal lobe structures, but additional cognitive deficits that occur early in the course of AD contribute to the observed reduction of their primacy effect. For example, very mild AD patients may have an early language impairment that precludes the normal verbal rehearsal that is necessary for the manifestation of the primacy effect. An interesting test of this possibility would be to examine the serial position effect in individuals who are in a preclinical stage of AD that is limited to a mild secondary memory deficit.

It is also possible that demographic factors may have contributed to the differences between the very mild AD and ECT groups. The ECT group was significantly younger than the very mild AD group and was composed only of men, thus it is possible that these factors rendered the ECT group better able to compensate for their amnesia than the very mild AD group. Nevertheless, further examination of the serial position effect and its relationship to the secondary memory deficits induced by very early AD or ECT is clearly warranted.

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