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WORD REPETITION EFFECTS ON EVENT-RELATED POTENTIALS IN HEALTHY YOUNG AND OLD SUBJECTS, AND IN PATIENTS WITH ALZHEIMER-TYPE DEMENTIA

MICHAEL D. RUGG,* STEPHANIE PEARL,† PAMELA WALKER,† RICHARD C. ROBERTS† and JULIET S. HOLDSTOCK*

Wellcome Brain Research Group, *School of Psychology, University of St Andrews, St Andrews, Fife, U.K.; †Department of Medicine, University of Dundee, and Division of Clinical Neurosciences, Dundee Royal Infirmary, Dundee, U.K.

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Abstract—Event-related potentials (ERPs) were recorded from 16 healthy young (mean age 21 years) and 16 healthy old subjects (mean age 64 years), and from 11 subjects with a diagnosis of Dementia of Alzheimer Type (DAT). The task requirement was to attend to a series of visually presented words so as to respond to occasional animal names. Non-animal names repeated after either a single or six intervening items. In the young subjects ERPs evoked by repeated words displayed a widespread, sustained positive-going shift relative to ERPs evoked by first presentations (the ERP repetition effect). This effect onset around 220 msec and did not differ as a function of inter-item lag. Other than for a delay in onset of approximately 80 msec, the ERP repetition effect in the healthy old group was in all respects equivalent to that of the young subjects. The ERP repetition effects in the DAT patients were statistically indistinguishable from those of an appropriately matched sub-set of the healthy old subjects.

These results indicate that the ERP repetition effect remains robust in subjects in whom explicit memory has declined as a result of normal aging or DAT. Thus they suggest that the effect reflects processes independent of those underlying explicit memory, and that it may index a form of memory relatively unaffected by the pathology underlying DAT.

INTRODUCTION

THE last few years have seen an upsurge of interest in event-related potential (ERP) studies of memory [31]. A number of these studies have investigated ERPs evoked by 'old' and 'new' words during direct tests of recognition memory [1, 5, 14, 17, 26, 28, 34, 37, 41]. Other studies have employed indirect memory tests in which word (and non-word) repetition was incidental to the task (e.g. Refs [2], [15], [23], [32], [33], [36], [38]). The basic finding, common to both types of memory test, is that when item repetition occurs over intervals of less than a few minutes, ERPs evoked by old (i.e. repeated) items are more positive-going than those evoked by new ones. This phenomenon is sometimes called the 'ERP repetition effect'.

The ERP repetition effect reflects the modulation of multiple ERP components, which have been dissociated as a function of the interval between first and second presentations [33, 37], and word frequency [33, 43]. It has been suggested that the components underlying the effect include the well-researched N400 (attenuated by word repetition) and P3 (enhanced by repetition) components. The relative contributions of these two components to the repetition effect appears to vary according to task and stimulus characteristics [35].

The functional significance of the ERP repetition effect is unknown. Although it is found with indirect memory tests—the kind of test typically employed to study "priming" and other manifestations of implicit memory [29]—it has been argued [31] that the effect reflects, at most, only a subset of the processes that contribute to implicit memory. The principal ground for this argument is that the longevity of word repetition effects on behaviour far exceeds the longevity of such effects on ERPs. Nonetheless, it seems doubtful whether the effect, or at least that part of it attributable to the modulation of the N400, reflects processes necessary for the explicit recognition of old items. RUGG and NAGY [37] found that differences between ERPs evoked by old and new words were attenuated and delayed in onset when the study-test interval increased from approximately 1 to 45 min, although recognition memory remained good at the longer interval.

The absence of a relationship between the ERP repetition effect and processes subserving explicit memory is also attested by neuropsychological evidence. RUGG *et al.* [39] found that when repetition was immediate, the ERP repetition effect was unaffected in patients who had undergone left (or right) anterior temporal lobectomy, implying that the effect is not dependent on the integrity of temporal lobe structures necessary for normal verbal memory. RUGG *et al.* (Ref. [39]; see also Ref. [41]) found however that temporal lobectomy was associated with abnormally small differences between old and new words in a continuous recognition test, in which repetition occurred after about six intervening items. This finding was taken as evidence that the effects of repetition on ERPs were dependent on the temporal lobe when items must be retrieved from long-term memory in order to be explicitly recognised. Possible reasons for the difference in the sensitivity to temporal lobe damage of RUGG *et al.*'s [39] repetition and continuous recognition procedures are addressed in the Discussion.

If the ERP repetition effect is independent of the cognitive processes and neural structures specifically subserving explicit memory, it should be normal in other groups in whom explicit memory is poor. A considerable body of evidence suggests that explicit memory shows a more marked decline with age than implicit memory does (e.g. Ref. [10]). The reasons for age-related changes in memory function are unclear [21]. Nonetheless, the comparison of ERP repetition effects in young and old subjects affords the opportunity to assess whether these effects, as with measures of explicit memory, decline with age.

Memory in the normal elderly is of course much better than that in similarly aged individuals in whom memory function is compromised as a result of Dementia of Alzheimer Type (DAT). Early in the course of this disease memory impairment is most marked on tests of explicit memory, with relatively preserved performance on at least some indirect tests that assess implicit memory for the same material (see Refs [9] and [24] for reviews). DAT thus provides an opportunity to study ERP repetition effects in the context of a considerably more profound deficit of explicit memory than that which occurs in the healthy elderly.

Few studies have as yet studied ERP repetition effects in either normal old subjects or those with DAT. Friedman and colleagues have reported two studies in which the effects of word repetition on ERPs were compared in young and old subjects [8, 11], and a further study in which groups of young, old and DAT patients were studied (Ref. [7], see Ref. [6] for a summary and additional analyses). In all of these studies, the critical task involved semantic judgements (detection of animal names) on a series of visually-presented words, some of which repeated after either 2, 8 or 32 intervening items [8, 11], or after an average of 14 items (Ref. [7]; range unspecified). In HAMBERGER and FRIEDMAN [11] a speeded response was required to all items, whereas in FRIEDMAN *et al.* [7] and FRIEDMAN *et al.* [8], as in most

previous work on the ERP repetition effect, responses were made only to occasional "target" items (the animal names), and were withheld to the items of experimental interest. The effects of repetition in young and healthy old subjects in the HAMBERGER and FRIEDMAN [11] study were of similar magnitudes, time-courses and scalp distributions, while in FRIEDMAN *et al.* [7] and FRIEDMAN *et al.* [8] the effects in the old group were slightly delayed in onset, but larger and more sustained than in the younger subjects. No lag effects were found in any study. Clearly, these data offer no support for the view that the ERP repetition effect declines with age.

A similar conclusion emerged from the study of KARAYANIDIS *et al.* [16], who investigated age effects on ERPs evoked by word repetition in two versions of a lexical decision task. Karayanidis *et al.* found that although ERP repetition effects in their oldest group onset and peaked later than in young subjects, the effects were equivalent in amplitude and more prolonged in the older subjects. These age-related differences were more pronounced when repetition occurred after four intervening items than when it was immediate.

FRIEDMAN *et al.* [7] reported that DAT patients showed ERP repetition effects that were statistically indistinguishable from those of their age-matched controls. Assuming that the ERP repetition effect reflects the same processes as those responsible for the implicit effects of word repetition on behaviour, FRIEDMAN *et al.* [7] concluded that their results were consistent with other findings that at least some forms of implicit memory are preserved in early DAT. They noted however that despite the absence of statistical evidence for abnormal ERP repetition effects in their DAT patients, several patients failed to show such effects. FRIEDMAN *et al.* [7] speculated that these were individuals in whom the disease had compromised neural structures underpinning implicit memory.

The present study follows on the findings of FRIEDMAN and colleagues and KARAYANIDIS *et al.* [16] by comparing ERP repetition effects both in healthy young and older subjects, and also in older subjects who are healthy or who have received a diagnosis of DAT. The aim was first, to establish the generality of the findings described above, and second, to examine in more detail than hitherto the relationship between the ERP repetition effect and explicit memory performance. The study employed a task similar to that used by FRIEDMAN *et al.* [7] and in previous studies of the ERP repetition effect in young subjects (e.g. Ref. [38]). To follow up the hint from RUGG *et al.* [39] that the effect may be sensitive to the interaction of inter-item lag with subject variables, two lags, of similar lengths to those used in that study, were employed.

METHOD

Subjects

Subjects consisted of 16 young adults, 16 old individuals and, initially, 16 DAT patients. Five subjects from this last group were rejected; four because of their inability to perform the experimental task, and one because of technically inadequate ERP recordings. All the young and healthy old subjects reported that they were in good health and had no history of neurological disease. The DAT patients fulfilled the NINCDS criteria for diagnosis of probable Alzheimer's disease. They all had progressive insidious onset of symptoms, no history of stroke, and no abnormal neurological signs other than cognitive impairment. The main complaint was worsening of memory of at least 1 year's duration. They had no other active medical problems and were taking no medication with CNS activity. CT scans were either normal for age or showed generalised cerebral atrophy. CSF examinations were not performed. Selected characteristics of each group are summarised in Tables 1 and 2. The second of these tables describes only the 11 DAT patients who contributed ERP data, along with the 11 old subjects most closely matched to them on the combined criteria of age, sex, and pre-morbid IQ (as measured by the National Adult Reading Test [25]).

Table 1. Characteristics of the young ($N = 16$) and old ($N = 16$) healthy subjects

	Young	Old	
AGE			
Mean	20.7	63.8	
S.D., range	3.0, 16–26	4.6, 57–75	
NART*			
Mean	109.9	114.0	
S.D., range	6.5, 100–120	4.7, 102–122	
Paired Associate†			
Easy			
Mean	11.6	11.1	n.s.
S.D., range	0.6, 10–12	1.1, 9–12	
Hard			
Mean	9.1	5.1	$P < 0.001$
S.D., range	1.7, 6–11	3.0, 0–10	
ADAS recall‡			
Mean	23.0	18.6	$P < 0.005$
S.D., range	2.8, 17–29	4.3, 10–25	
ADAS recognition§			
Mean	33.4	30.8	n.s.
S.D., range	2.1, 29–36	4.7, 17–36	

*National Adult Reading Test.

†Verbal Paired Associate Learning sub-test of the WMS–R.

‡Sum of recall after each of three presentations of a visually presented 10-word list.

§Hits-false alarms. Summed over three test lists consisting of the same study set of 12 words mixed with 12 distractors new to each list. One young subject did not perform this test.

Memory tests

Three direct tests of verbal memory were administered. These were the word recall and word recognition tests of the Alzheimer's Disease Assessment Scale (ADAS [30]), and the verbal paired associates test of the Wechsler Memory Scale–revised (WMS–R).

ERP task

Stimuli: The stimuli comprised 421 English words, 80 of which were animal names (targets). Of the remainder, 21 were presented once only, 80 were presented twice separated by one intervening item (lag 1 repeats), and 80 were presented twice separated by six other items (lag 6 repeats). The non-targets varied in length between 3 and 8 letters (mean 4.9), and had a mean frequency of occurrence [20] of 129 per million. Two stimulus lists were constructed. These employed the same pseudo-random ordering of targets, unrepeated items, and first and second presentations of lag 1 and lag 6 repeats. They differed however in their assignment of items to conditions: items employed for lag 1 repeats in one of the lists were used for the lag 6 condition in the other, and vice versa. A practice list of 43 items was also constructed.

The stimuli were presented on a TV monitor (white on black) for a duration of 300 msec, with an inter-stimulus interval of 3.3 sec. The stimuli subtended a vertical angle of approximately 0.3°, and a maximum horizontal angle of 1.5°. Other than for a 1400 msec period, beginning 100 msec before stimulus onset, a fixation asterisk was continuously displayed.

Procedure

Following electrode application, subjects were seated in front of the TV monitor, and were given a thumb-switch to hold in their preferred hand. They were informed that they would see a sequence of words appearing on the monitor, that they should silently read each word when it appeared, and that they should respond by squeezing the switch as quickly as they could whenever the word was the name of an animal. They were further instructed to maintain fixation on the asterisk, and to avoid blinking whenever the asterisk was absent from the screen. Following the instructions, subjects were given the 43 practice trials. These were repeated as necessary to allow subjects fully to comprehend and familiarise themselves with the task.

Table 2. Characteristics of the DAT patients ($N = 11$) and matched old control subjects ($N = 11$)

	Old	DAT	
AGE			
Mean	64.9	68.5	
S.D., range	5.1, 57–75	7.1, 55–77	
NART			
Mean	113.6	108.6	
S.D., range	5.5, 102–122	7.7, 99–119	
MMS*			
Mean	28.0	20.6	$P < 0.001$
S.D., range	1.5, 25–30	3.3, 15–24	
Paired Associate			
Easy			
Mean	10.7	6.7	$P < 0.005$
S.D., range	1.2, 9–12	3.5, 1–12	
Hard			
Mean	4.9	0.6	$P < 0.001$
S.D., range	3.2, 0–9	0.7, 0–2	
ADAS recall			
Mean	17.8	11.2	$P < 0.001$
S.D., range	4.4, 10–24	3.3, 6–16	
ADAS recognition			
Mean	31.5	23.7	$P < 0.01$
S.D., range	5.1, 17–36	7.3, 12–34	

*Short version of the mini-mental state examination [4].

ERP recording

ERPs were recorded from 10 channels using tin electrodes. Nine of these electrodes were embedded in a proprietary electrode cap (Electro-cap International, Dallas, U.S.A.), and were sited using the 10–20 system [13] at Fz, Cz, Pz, at lateral frontal (50% of the distance from F3 to F7 and F4 to F8), temporal (50% of the distance from C3 to T3 and C4 to T4), and parietal (50% of the distance from P3 and T5 and P4 to T6) sites. The tenth electrode was situated on the right mastoid. All EEG recordings were referred to the left mastoid. ERPs were algebraically reconstructed offline to represent recordings with respect to a linked mastoid reference. Bipolar horizontal and vertical EOG were recorded from electrode pairs placed on the outer canthus of each eye (horizontal), and on the infra- and supra-orbital ridges of the left eye (vertical). All channels were recorded with a bandpass of 30 −0.03 Hz (3 dB points) and were sampled at a rate of 4 msec/point, starting 100 msec before stimulus onset and continuing for 1024 msec.

ERPs were formed to first and second presentations of repeated words by averaging all error-free trials which were also free of EOG artefact. In subjects in whom blinks were so frequent as to lead to one or more of the resulting ERPs to be formed from less than 20 trials, an EOG correction procedure was employed. This procedure was based on a combination of the approaches advocated by O'Toole and Iacano [27] and Semlitsch *et al.* [40].

RESULTS

The data from the young and healthy old groups are first described and analysed. The data from the DAT patients are then compared to those from their 11 matched controls.

Young vs Healthy

Memory tests. Scores on the tests of paired associate learning, word recall and word recognition are summarised in Table 1. The performance of the old subjects was both more variable and significantly worse than that of the young group on the hard paired associate and word recall tests.

ERP task performance. Mean RT, and standard deviation of the RT distributions, along with number of correct detections and false positive responses are summarised in Table 3.

Table 3. Mean reaction time (msec), standard deviation of reaction time, percentage of correct detections (CD) and percentage of false alarms (FA) for the young ($N = 16$) and old ($N = 16$) subjects

	Young	Old	
RT	615.9	675.5	n.s.
S.D.	112.3	85.0	
RT S.D.	132.4	115.4	n.s.
S.D.	41.7	29.8	
% CD	93.6	95.9	n.s.
S.D.	7.6	2.5	
% FA	8.2	9.6	n.s.
S.D.	5.5	5.8	

None of these meaures differed significantly as a function of group.

ERP waveforms. Figure 1 illustrates the grand average waveforms of the 16 subjects in each group, while grand average subtraction waveforms (repeats minus first presentations) are shown in Fig. 2. Figure 3 presents the two groups' subtraction waveforms from the Cz electrode site (where repetition effects were largest) in more detail. Five of the young subjects' waveforms were subjected to EOG correction, and seven of the old subjects' ERPs were similarly corrected. Means of 64 (range 45–78), 67 (47–78) and 64 (46–75) trials formed the ERPs evoked respectively by first presentations, lag 1 and lag 6 repetitions in the young subjects; the corresponding means for the old subjects were 63 (35–77), 63 (31–78), and 63 (29–78) trials.

Turning first to the young subjects, the ERPs evoked by repeated items display the characteristic positive-going shift seen in numerous previous studies (see Introduction). This shift—the ERP repetition effect—begins around 200–250 msec post-stimulus and continues until approximately 700 msec. The repetition effect seems equivalent in the two lag conditions, with the possible exception of the frontal electrodes, where it appears to be somewhat later in onset following repetition over the longer lag. The waveforms of the old group are similarly sensitive to word repetition. This is especially apparent from Figs. 2 and 3, where it can be seen that apart from an apparent delay in onset of around 100 msec relative to the young subjects, the old group's repetition effects appear similar in magnitude, scalp distribution and insensitivity to lag.

The ERP data were analysed in two stages. To establish that the effects of repetition in each group were statistically significant, ANOVAs were conducted on the mean amplitude of 300 msec regions of the waveform roughly straddling the latency at which the effects were at their largest. These regions were 300–600 msec in the young group, and 400–700 msec in the older subjects. In each case (and for all other mean area measurements) amplitude was determined with respect to the mean of the 100 msec pre-stimulus baseline. For each group, the ANOVAs employed the factors of condition (first presentation, lag 1 repetition, lag 6 repetition), electrode 'chain' (midline, left hemisphere, right hemisphere), and electrode site (frontal, central/temporal, and parietal). The ANOVAs were followed by planned comparisons contrasting first presentations with lag 1 and lag 6 repetition. Degrees of

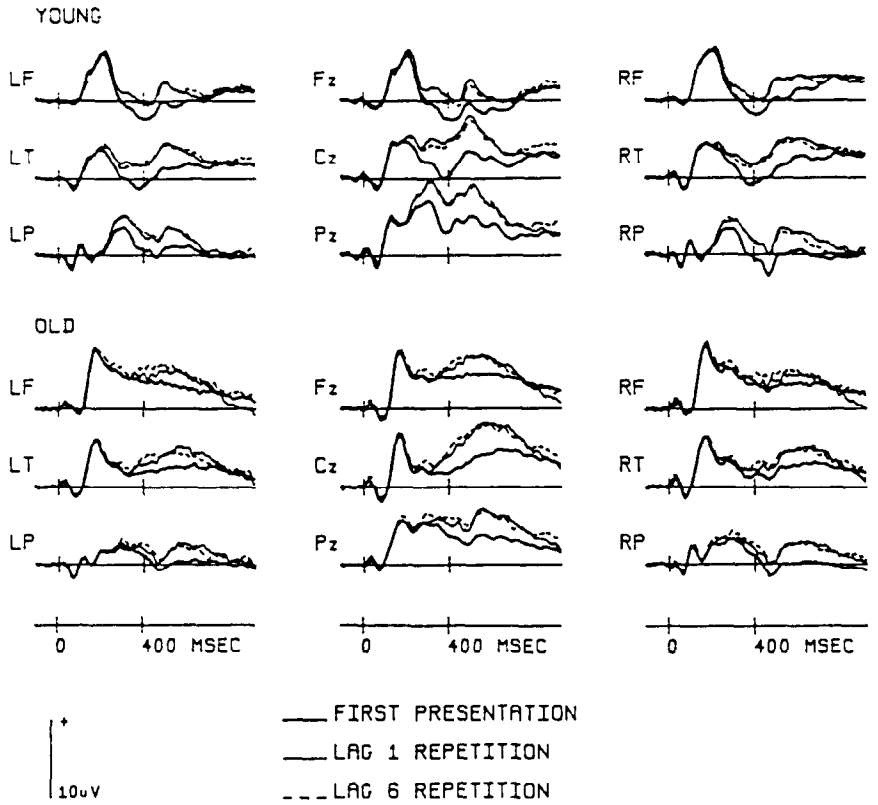

Fig. 1. Grand-average waveforms evoked by first presentations, lag 1 and lag 6 repetitions in young ($N = 16$) and old ($N = 16$) subjects. Fz, Cz, and Pz refer to frontal, central and parietal midline sites. LF, RF, LT, RT, LP, and RP refer to left and right frontal, temporal and parietal sites.

freedom were adjusted when appropriate with the Geisser Greenhouse procedure to correct for non-sphericity [19].

Inter-group comparisons of ERPs were made on measures derived from subjects' subtraction waveforms. These analyses thus allowed a direct comparison of the magnitude and scalp distribution of the lag 1 and lag 6 repetition effects in each group (the focus of the study) independent of other differences between the ERPs of the two groups. Analyses of two aspects of the data were conducted. Onset latencies of the repetition effects were estimated by computing, across subjects, point-by-point t-tests against the null hypothesis of zero difference from baseline. To maximise the stability of these estimates, they were computed on the weighted averages of the waveforms from each repetition condition. The onset latency at a given electrode site was defined as the latency at which a t-value attained significance at the 0.05 level or better, and was followed by at least another 25 consecutively significant values.

Second, measures of the region of the waveforms in which the repetition effects were at their largest were contrasted. An ANOVA was conducted contrasting the mean amplitude of the 300-600 msec region of the young subjects with the 400-700 msec region of the old group. The ANOVAs employed the factors of group, lag, electrode chain, and electrode site. Finally, the scalp distributions of the repetition effects of the two groups were compared. This analysis was carried out on the amplitudes of the 300-600 msec (young) and 400-700 msec

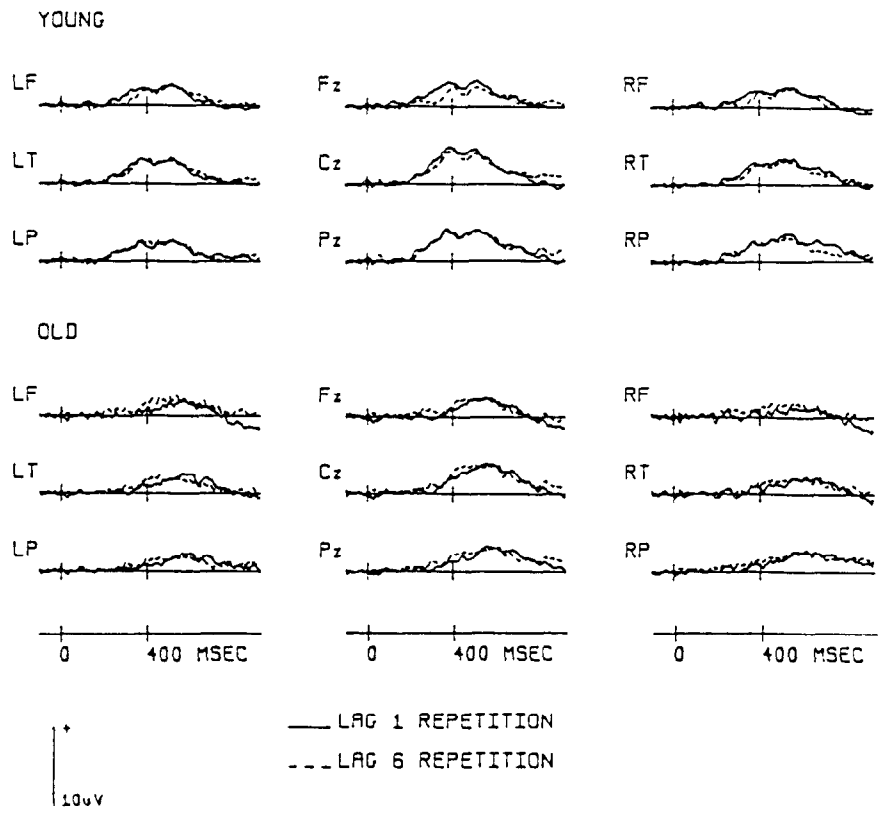

Fig. 2. Grand-average subtraction waveforms of the ERPs from the young ($N = 16$) and old ($N = 16$) subjects. Waveforms were formed by subtracting the ERPs evoked by first presentations from those evoked by lag 1 and lag 6 presentations. Electrode sites as in Fig. 1.

(old) latency regions after rescaling using the procedure recommended by McCARTHY and WOOD [22].

In describing the outcome of these various ANOVAs, effects involving the factors of site and hemisphere are noted only when they interact with experimental condition or group, since these factors are in themselves of no theoretical interest in the context of this study.

ANOVA of the 300–600 msec latency region of the young subjects' ERPs revealed a main effect of condition [$F(1.9, 28.0) = 19.40$, $P < 0.001$], and an interaction between condition and chain [$F(2.9, 43.5) = 8.20$, $P < 0.001$]. Planned comparisons revealed that, collapsed over chain and site, ERPs evoked in both the lag 1 and lag 6 conditions were significantly more positive than those to first presentations. The condition by chain interaction arose because repetition effects were larger over midline than lateral sites.

ANOVA of the 400–700 msec latency region of the old group's ERPs yielded a similar outcome. There was a significant effect of condition [$F(1.8, 27.0) = 13.17$, $P < 0.001$], and an interaction between condition and chain [$F(3.0, 44.5) = 10.13$, $P < 0.001$]. Planned comparisons revealed that lag 1 and lag 6 ERPs were significantly more positive than ERPs to first presentations. As for the young subjects, the condition by chain interaction reflected larger repetition effects over the midline.

Onset latencies of the repetition effects (pooled over lag; see above) at the Cz electrode

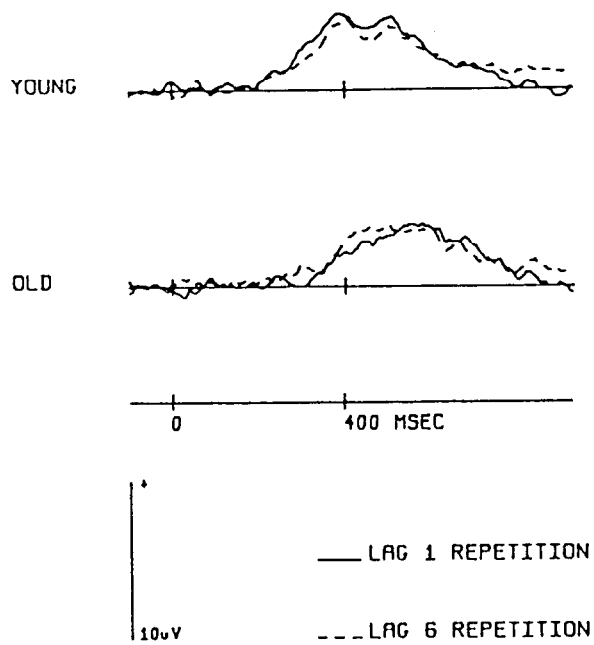

Fig. 3. Grand-average subtraction waveforms from the Cz electrode site of the young ($N = 16$) and old ($N = 16$) subjects.

(where the effects were largest in both groups) were 220 msec for the young subjects, and 300 msec for the old group. Similar differences in onset between the two groups were found at the other electrode sites.

The mean amplitude of the 300–600 (young and 400–700 msec (old) latency regions of the subtraction waveforms are shown in Table 4. ANOVA failed to reveal any significant effect

Table 4. Mean amplitude (μV) of the ERP repetition effect, collapsed over lag, for the 300–600 msec latency region in the young subjects ($N = 16$) and the 400–700 msec region in the old subjects ($N = 16$)

	FZ	CZ	PZ	LF	LT	LP	RF	RT	RP
Young									
Mean	2.2	3.6	3.4	1.9	2.6	2.2	1.8	2.5	2.5
S.D.	2.7	2.4	2.5	2.2	2.2	2.4	2.2	1.8	2.0
Old									
Mean	1.9	3.3	2.5	1.6	1.7	1.6	1.2	1.7	2.1
S.D.	2.2	2.2	1.8	2.7	2.0	1.6	1.9	1.7	1.9

involving the factors of group, indicating that these measures were of equivalent size and scalp distribution in the two groups. The similarity of the scalp distribution of the repetition effects is further attested by the outcome of the ANOVA on the rescaled data. Once again, no effects involving the factor of group were obtained.

In summary, young and old groups both displayed highly reliable repetition effects, which differed minimally with inter-item lag. The old subjects' effects were equivalent in both

magnitude and scalp distribution to those of the young group, although delayed by approximately 80 msec.

DAT vs Healthy old subjects

Memory performance. Mean scores of the two groups on the tests of paired associate learning, free recall and recognition are shown in Table 2. The DAT patients performed at a significantly lower level than their controls on all three tests.

ERP task performance. Mean target RT, RT variability, and accuracy measures are shown in Table 5. Although not significantly longer, the DAT patients' RTs were more variable than

Table 5. Mean reaction time (msec), standard deviation of reaction time, percentage of correct detections (CD) and percentage of false alarms (FA) for old controls ($N = 11$) and DAT patients ($N = 11$)

	Old	DAT	
RT	682.6	743.9	n.s.
S.D.	100.1	122.9	
RT S.D.	119.5	153.0	$P < 0.05$
S.D.	33.9	34.1	
% CD	95.8	85.9	$P < 0.05$
S.D.	2.2	12.5	
% FA	9.9	12.2	n.s.
S.D.	5.4	8.4	

those of the controls. The patients also detected fewer targets, although they did not make more false positive responses.

ERP waveforms. The DAT group's grand average waveforms, along with those of the 11 matched old controls, are shown in Figs 4, 5 and 6. A repetition effect is clearly evident in the DAT subjects' waveforms. This appears to onset around 300–400 msec post-stimulus, and initially to be of similar magnitude for both lags. From 400 msec onwards, however, the effect appears to be smaller in the longer lag condition. As in the control group, the 300 msec region between 400 and 700 msec roughly straddles the regions in which the repetition effects are at their maximum.

Six of the controls', and 10 of the DAT patients' waveforms were subjected to EOG correction. Means of 63 (range 35–77), 63 (31–76), and 64 (29–78) trials formed the ERPs evoked respectively by first presentations, lag 1 and lag 6 repetitions in the controls, while in the DAT subjects the corresponding means and ranges were 66 (range 52–76), 66 (56–77), and 67 (53–74).

The analyses of the DAT patients' ERPs focused not only on the question of whether, as a group, they exhibited reliable repetition effects, but also on the consistency of these effects across individual subjects. Two latency windows, spanning 300–400 msec and 400–700 msec were selected for analysis. The earlier of these windows was chosen since it encompasses the region of the waveform in which repetition effects first emerge in these subjects according to the grand average waveforms shown in Figs 4 and 5. The second region straddles the region of the subtraction waveforms in which the effects were maximal. The repetition effects of the DAT patients in each latency region were analysed to evaluate both their within-group reliability, and their comparability with those of the control group.

The repetition effects of the DAT patients and controls in the 300–400 msec and 400–700

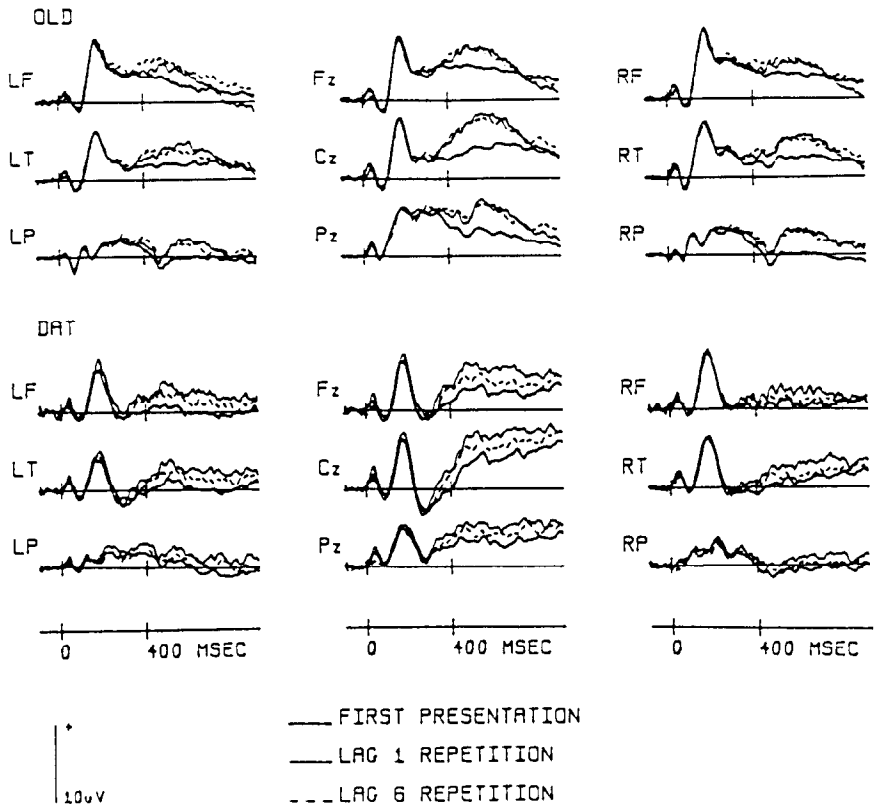

Fig. 4. Grand-average waveforms evoked by first presentations, lag 1 and lag 6 repetitions in the DAT patients ($N = 11$) and old controls ($N = 11$). Electrode sites as in Fig. 1.

msec latency regions are shown in Table 6, and are plotted individually in Fig. 7 for the Cz electrode site. As can be seen from this figure, in the earlier of these regions the ERPs of the overriding majority of the patients are more positive-going when evoked by repetitions of either lag, and are of equivalent size in the two lags. In the later region, the effects tend to be smaller at the longer lag, but are nonetheless consistently positive-going. Thus the apparent difference between lags in the DAT patients' grand average waveforms in Figs 4–6 does not reflect increased inter-subject variability at the longer lag.

t-Tests revealed that the DAT patients' repetition effects illustrated in Fig. 7 were, in every case, significantly different from zero (300–400: lag 1, $t_{10} = 3.89$, $P < 0.01$, lag 6, $t_{10} = 3.14$, $P < 0.01$; 400–700: lag 1, $t_{10} = 4.38$, $P < 0.005$, lag 6, $t_{10} = 4.90$, $P < 0.001$). Consistent with these findings ANOVA (factors of condition, chain and site) of the 400–700 msec region of the DAT patients' ERPs revealed a significant effect of condition [$F(1.4, 13.6) = 9.77$, $P < 0.005$]. Planned comparisons revealed that the ERPs from both repetition conditions (collapsed over chain and site) were more positive than those evoked by first presentations. A second ANOVA conducted on the data from the two repetition conditions alone did not show any significant effects involving the factor of condition.

The magnitudes and scalp distributions of the repetition effects from the DAT patients and their controls were contrasted with ANOVAs of both raw and rescaled measures of the

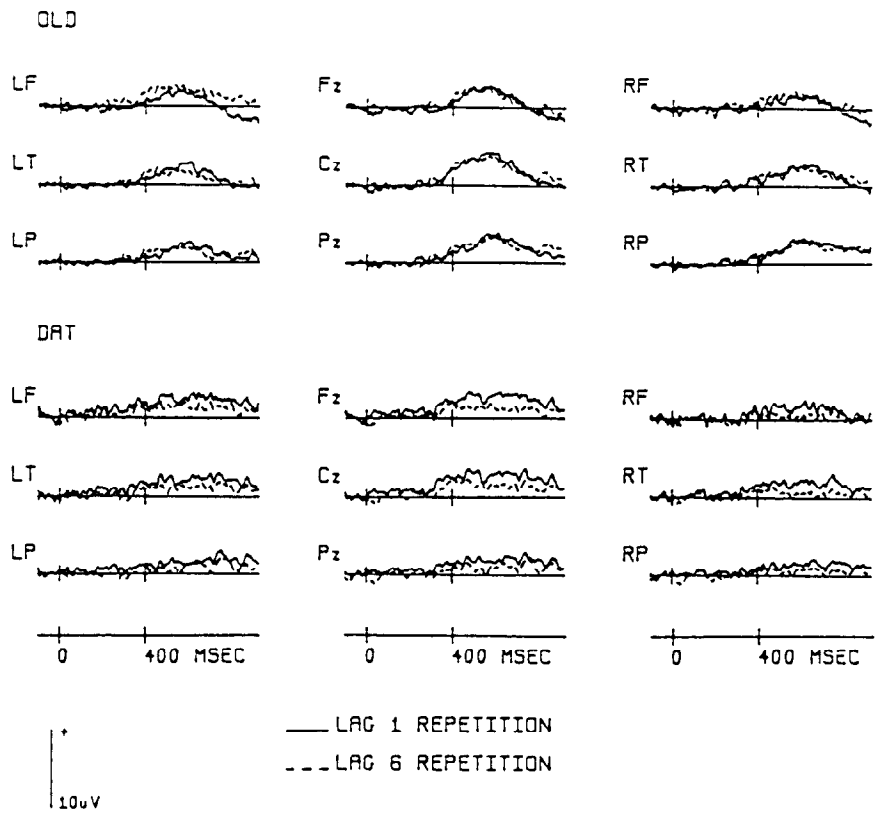

Fig. 5. Grand-average subtraction waveforms of the ERPs from the DAT patients ($N = 11$) and old controls ($N = 11$). Details of subtractions as for Fig. 2. Electrode sites as in Fig. 1.

400–700 msec latency region of their subtraction waveforms. In neither case did any effect involving the factor of group attain or approach significance. Hence, this region of the two groups' repetition effects was statistically indistinguishable with respect to both magnitude and scalp distribution.

In summary, the effects of repetition on the ERPs of the DAT subjects were not only statistically significant, but highly consistent over subjects. The onset latencies, magnitudes and scalp distribution of these subjects' effects were statistically indistinguishable from those of their age-matched controls. Furthermore, we found no evidence that the magnitude of the effects covaried with measures of explicit memory, or indeed with more general measures of severity of illness such as those given by the Mini-Mental State questionnaire or total ADAS score.

DISCUSSION

These findings agree with those of HAMBERGER and FRIEDMAN [11] in failing to show a reduction in the magnitude of ERP repetition effects in the normal elderly, but differ from other studies [7, 8, 16] in that they also failed to show enhanced effects in these subjects. Any number of factors may lie behind this inconsistency between studies, including differences in subject samples, details of experimental procedure (e.g. number of inter-item lags employed),

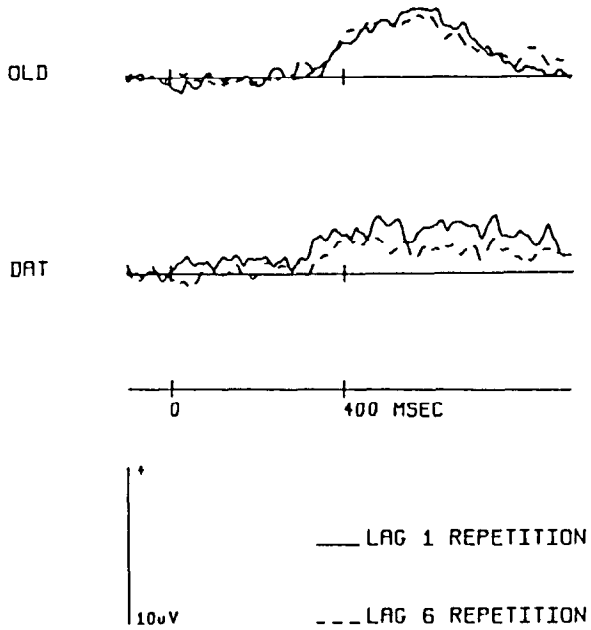

Fig. 6. Grand-average subtraction waveforms from the Cz electrode site of the DAT patients ($N = 11$) and old control subjects ($N = 11$).

Table 6. Mean amplitude (μV) of the ERP repetition effect, collapsed over lag, of the 300–400 msec and 400–700 msec latency regions in old controls ($N = 11$) and DAT patients ($N = 11$)

	FZ	CZ	PZ	LF	LT	LP	RF	RT	RP
300–400									
Old									
Mean	0.1	0.9	0.9	0.5	0.5	0.6	0.2	0.6	0.8
S.D.	1.8	1.6	1.4	1.8	1.5	1.2	1.6	1.2	1.3
DAT									
Mean	1.3	1.6	0.8	1.2	0.9	0.4	0.5	0.8	0.4
S.D.	1.6	1.5	1.4	2.3	1.2	1.0	1.2	1.3	1.0
400–700									
Old									
Mean	1.9	3.3	2.7	1.7	1.7	1.7	1.3	2.0	2.2
S.D.	2.4	2.5	2.1	3.1	2.1	1.8	2.2	2.0	2.2
DAT									
Mean	2.1	2.4	1.5	2.0	1.7	1.1	1.1	1.4	1.1
S.D.	1.8	1.9	1.7	2.6	1.8	1.2	1.5	1.7	1.3

etc. FRIEDMAN *et al.* [8] interpreted their finding of an age-related enhancement of the ERP repetition effect as evidence that old subjects engage in more extensive processing of repeated items than young subjects. Evidently, this was not the case in the present study.

The present results are however in accord with those of Friedman and colleagues in failing to find evidence of an interaction between ERP repetition effects and inter-item lag. These

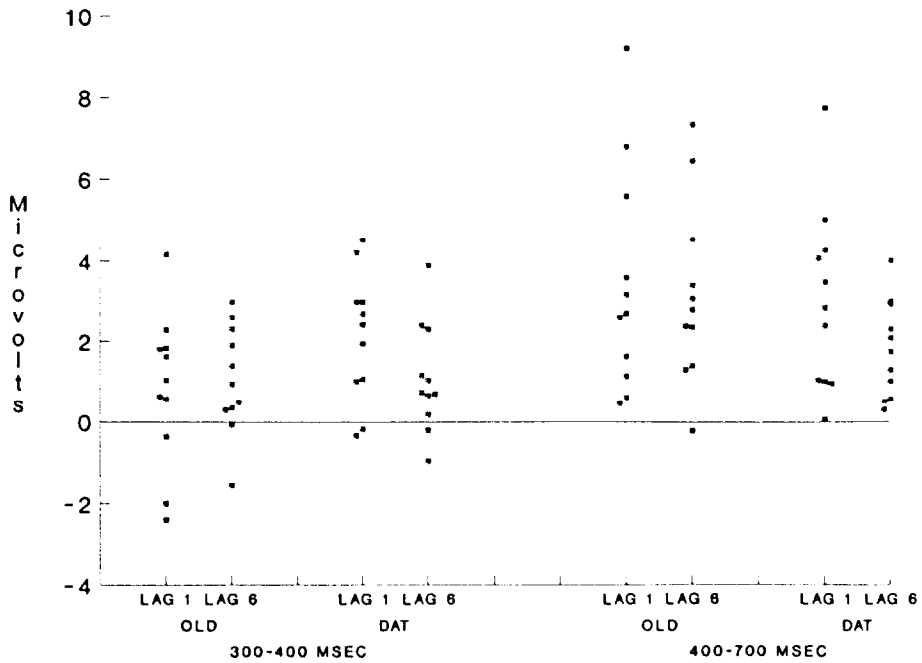

Fig. 7. ERP repetition effects from the Cz electrode site in the 300–400 msec and 400–700 msec latency regions of each DAT patient and control subject.

results contrast with those of KARAYANIDIS *et al.* [16] who not only reported such an interaction (see also Ref. [15]), but found that it varied with age. One possible reason for this discrepancy lies in the fact that KARAYANIDIS *et al.* [16] employed as their shortest 'lag' immediate repetition; the present study and those of Friedman and colleagues always had at least one item intervening between repeating items. This is unlikely to be a complete explanation though. The studies on young subjects of BENTIN and PELED [2] and NAGY and RUGG [23] each contrasted the effects of immediate and delayed word repetition during lexical decision and, in contrast to KARAYANIDIS *et al.* [15, 16], failed to find a lag by repetition interaction.

Other than for a delay in onset of approximately 80 msec, the repetition effects in the old subjects were indistinguishable from those of the young group. This finding stands in contrast to the fact that scores on the tests of paired associate learning and free recall were more variable and significantly lower in the old subjects. This dissociation between ERP and behavioural data is consistent with other work, noted in the Introduction, suggesting that ERP repetition effects are independent of the processes responsible for explicit memory.

Although differing on the two recall tests, the old and young subjects did not differ significantly on the recognition memory test, a finding consistent with previous work showing that age-related explicit memory impairments are more evident in tests of recall than recognition (reviewed by Ref. [3]). It raises the possibility that the normal ERP repetition effects in the old subjects reflect the same (relatively intact) processes responsible for the good recognition performance of these subjects. However, the findings from the DAT patients indicate that good recognition memory is not necessary for the emergence of normal ERP

repetition effects. This group was impaired on both recall and recognition, but nonetheless demonstrated reliable repetition effects.

Figures 4–6 suggest that the repetition effects at lag 6 are somewhat reduced in the DAT patients relative both to their lag 1 effects, and the lag 6 effects of the control group. Although this trend failed to attain statistical significance, it signals the need for caution before concluding that ERP repetition effects remain normal in DAT patients as inter-item lag increases. Two points are worth noting however. First, any reduction in the magnitude of the DAT patients' lag 6 repetition effects appears confined to the later part of the effects, which in the 300–400 msec latency range show little sign of differing from those of the control group. Second, in the 400–700 msec latency region, when the apparent reduction in the DAT patients' lag 6 effects is prominent, the effects are still highly reliable. Thus, even if not functioning entirely normally in DAT, the generators of ERP repetition effects nonetheless retain their sensitivity to word repetition when several items intervene between first and second presentations.

Although the neural basis of the decline in memory function that occurs during normal aging is unclear, the much more severe memory impairments observed in early DAT seem very likely to result from the pathology in the hippocampus and adjacent structures that forms a prominent and early manifestation of the disease [12, 42]. Thus the finding that ERP repetition effects can be normal in memory-impaired DAT patients suggests that these effects are not dependent on the normal functioning of these temporal lobe structures.

Normal ERP repetition effects have also been described after unilateral temporal lobectomy [39]. In one part of that study, a task similar to the one used here was employed, but repetition was immediate. On the basis of their findings with this task, RUGG *et al.* [39] suggested that ERP repetition effects are not dependent on the integrity of the anterior temporal lobe, a suggestion consistent with our present findings from the DAT patients. The present findings are however less easy to reconcile with the finding that words repeated in tests of repetition memory fail to modulate ERPs after unilateral temporal lobectomy [39, 41]. In Rugg *et al.*'s study for example, words were repeated after six intervening items, with the requirement explicitly to discriminate between first and second presentations. In contrast to the reliable lag 6 ERP repetition effects observed in the DAT patients in the present study, the ERPs of both left- and right-sided lobectomy patients failed to show reliable differences between 'new' and 'old' words. It is not possible at present to determine the reason for these seemingly disparate findings. One possibility is that, contrary to previous assumptions, ERP word repetition effects in direct and indirect tasks do not reflect equivalent cognitive processes. If so, lobectomy patients will show normal lag 6 ERP repetition effects when tested with the present procedure. Alternatively, the differences between DAT and lobectomy patients' long lag effects may reflect the contribution to these effects of regions of the temporal lobe that, while damaged or destroyed by lobectomy, are functionally competent in early DAT.

What light do these findings shed on the functional significance of ERP repetition effects? Given that the effects can be normal, or at least near normal, in the face of severe impairment of explicit, long term memory, it seems reasonable to conclude that they do not reflect this aspect of memory function. An alternative is that the effects reflect the functioning of a short-term memory (STM) system, which is relatively intact in both healthy old and DAT subjects. By this account, the normal repetition effects in these subjects occurred because a representation of each word's first presentation was still available in STM at the time of its second presentation. Hence a 'match' between first and second presentations could occur

without the need for retrieval from long-term memory. This account seems unlikely for several reasons. First, while it is plausible that a word would still be strongly represented in STM when it re-occurred in the lag 1 condition, this seems less likely for repeats occurring after six intervening items. Second, work with young normal adults has generally failed to find evidence of changes in the ERP repetition effects as a function of inter-item lag, as might be expected if effects over short and long lags depend upon retrieval from STM and LTM, respectively [2, 23]. Finally, FRIEDMAN *et al.* [8] reported that ERP repetition effects in their normal old subjects were equivalent for lags varying between 2 and 32 intervening items; the longer of these lags is far beyond the capacity of what is conventionally defined as STM.

An alternative account of ERP repetition effects is that, as suggested by FRIEDMAN *et al.* [7], they reflect processes subserving implicit memory, processes which are intact in both the normal elderly and in early DAT subjects. This account is appealing, in that it is consistent with the view that changes in memory function with age or as a consequence of DAT are more marked for explicit than implicit memory. It also fits well with the fact, noted by NEBES [24], that repetition priming effects on word identification are among the more robust of the implicit memory effects observed in DAT (e.g. Ref. [18]). There is however no direct evidence at present to support this account. Such evidence could be provided in the future by studying ERP repetition effects in DAT patients in whom measures of implicit memory function have been obtained. It would then be possible to determine whether any measure of implicit memory predicted the magnitude of ERP repetition effects. Such a finding would lend credence to the idea that these effects do indeed reflect processes contributing to implicit memory.

In summary, this study found that differences in explicit memory function between young, old, and DAT subjects were not accompanied by corresponding differences in the size of the ERP repetition effect. In addition, there was no evidence that the onset of the effect was delayed in DAT patients relative to their age-matched controls. Hence the effect may reflect cognitive, neural processes contributing to memory functions that are relatively insensitive to aging and early DAT.

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