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Automatic and Effortful Processing in Aging and Dementia: Event-Related Brain Potentials

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FORD, J. M., W. T. ROTH, B. G. ISAACKS, J. R. TINKLENBERG, J. YESAVAGE AND A. PFEFFERBAUM. *Automatic and effortful processing in aging and dementia: event-related brain potentials.* NEUROBIOL AGING **18**(2) 169–180, 1997.—Automatic and effortful processes were investigated using event-related brain potentials (ERPs) recorded from moderately impaired subjects with probable Alzheimer's Disease (AD), normal elderly, and normal young controls. The effects of effortful attention on ERPs to loud noises and the effects of stimulus intrusiveness on effortfully elicited ERPs were studied. First, ERPs to task relevant and irrelevant startling noises were compared. Second, ERPs to startling noises and moderate tones were compared when both were targets. The effects of age (young vs. elderly controls) and effects of dementing disease (AD subjects vs. elderly controls) were also assessed. Effortful attention augmented noise-elicited P300 amplitude in elderly subjects, but not in young. Intrusiveness augmented task-relevant P300 amplitude in young subjects, but not in elderly. Neither variable affected P300 amplitude in AD subjects. Thus, effects of age and disease depended on how P300 was elicited: when effortfully elicited, P300 amplitude was affected by disease but not age; when automatically elicited, P300 amplitude was affected by age but not disease. N1 effects differed from P300 effects. © 1997 Elsevier Science Inc.

Aging Dementia N1 P300 Reaction time Startle Blink ERPs Noise Target detection

EXPERIMENTAL evidence supports the theoretical distinction between effortful and automatic cognitive processes (40,49). Compared to effortful processes, automatic processes require minimal amounts of attentional capacity, and are relatively resistant to the influences of effort and concurrent tasks (48). Effortful processes are generally more vulnerable to aging (5,47) than are automatic processes (17). For example, noting the frequency of past events (17) and forming expectancies based on past events (7) occur automatically and are unaffected by aging.

An exception to this pattern is the automatically elicited response to loud, startling noises. Startling events make an immediate and automatic call on attention, drawing on essential resources (20,29). Cognitive event-related potential (ERP) data suggested that elderly subjects are relatively unresponsive to startling noises; startling noises elicited fewer startle blinks and a smaller-than-expected P300 component of the ERP (9,10). Although the elderly typically suffer from high-frequency hearing deficits, reduced responsiveness to loud noises in the elderly was not due to high-frequency hearing loss. Even after adjusting the noises to each subject's hearing threshold and narrowing the bandwidth of the noises, elderly subjects still had reduced responses to noises (10).

In Alzheimer's Disease (AD), automatic and effortful processes are affected to varying degrees depending upon the task. Typically, for AD subjects, automatic processes are relatively spared compared to effortful ones (17). Rohling et al. (43) used tasks involving the automatic registration of spatial location and frequency of occurrence, as well as effortful free-recall tests of memory. They found that both automatic and effortful task performance was impaired in AD patients, while multiinfarct dementia patients showed relatively spared automatic encoding. Strauss et al. (51) suggested that if automatic processes are impaired, stimuli normally encoded automatically can be encoded effortfully if sufficient resources can be made available.

ERPs are an on-line reflection of stimulus processing, from the earliest sensory responses to the later cognitive ones, and can be recorded in the total absence of overt behavior. N1 components (27) to relevant or target tones may reflect both attentional and sensory factors, while N1 to irrelevant, frequent, background tones may reflect primarily sensory factors. In spite of some dependence on sensory ability, N1 to both relevant and irrelevant tones tends to be larger in elderly than in young subjects (9). Only one study has used N1 to study AD. N1 to relevant tones (occurring on 20% of trials) was significantly smaller in AD subjects, although N1 to the frequent background tones was not (38). This pattern suggests that AD subjects suffer more from attentional than sensory deficits. N1 responses to startling noises in the elderly and AD subjects have not been assessed.

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The P300 component of the ERP represents a cognitive response to a change in the environment and is most commonly elicited by a rare or oddball event in a series of frequent background events. It has been interpreted as reflecting memory updating (3) or context closure (52). Because the eliciting event is not only rare but is usually also task relevant, P300 is typically elicited as part of the effortful process of responding to, or counting, a rare event (19). However, it can also be elicited by loud noises, automatically without a task (41,44). The scalp distribution of the P300 elicited by loud noises is not different from the P300 elicited by tones in a target detection task (10). The latency of the P300 peak is often considered to be a relative index of stimulus evaluation time, as it gets longer with more complex stimuli and task requirements (23).

AD reduces the amplitude (13) and increases the latency of P300 (13,28,30,34,38). Because of difficulties in getting demented patients to make the effortful responses required in most P300 paradigms, one study used an oddball paradigm without a target detection requirement and still found P300 latency differences between demented patients and age-matched controls (28). The P300 in this paradigm represented an automatically elicited cognitive process. Although startling noises also automatically elicit P300 (41,42), neither the amplitude nor latency of a noise-elicited P300 has been used to study automatic processes in AD.

Four hypotheses related to intrusiveness were tested: 1) Age-related P300 hyporeactivity to loud noises will be further reduced by dementia. Responses to task-relevant sounds that are intrusive (noises) and unintrusive (tones) were compared. A significant interaction between disease and intrusiveness for P300 amplitude was predicted. 2) N1 to task relevant rare tones and noises will follow the same pattern as P300 amplitude. Tests of this hypothesis followed those for P300. 3) N1 will reflect attentional dysfunction in the elderly and AD subjects, but will be insensitive to any sensory dysfunction. A significant reduction of N1 to rare events in older and AD subjects with no reduction in N1 to background tones was predicted. 4) P300 latency will be shorter to noises than to tones because the noises are louder and, hence, more arousing; this speeding will be greater in the elderly and AD subjects, because these groups tend to be underaroused. A significant main effect for intrusiveness and an interaction between group and intrusiveness for P300 latency were predicted. For all these hypotheses, intrusiveness was considered to be due to both quality (bandwidth) and intensity.

Two hypotheses related to task relevance were tested: 1) P300 responsiveness to loud noises can be augmented by effort, especially in elderly and AD subjects. Responses to noises when task relevant (button press) and irrelevant (no button press) were compared. An exaggerated effort-related increase in responsiveness in the elderly or demented would be seen in a significant interaction between task relevance and age and/or dementia for P300 amplitude. 2) P300 latency delay in the elderly and AD subjects is related to lack of effort. It was predicted that in elderly and AD subjects, but not in young subjects, P300 latency would be shortened by the requirement to make a button-press response to the noise. It should be noted that interpretations of the task relevance effect must take into account that task relevant noises occurred in a paradigm that always followed the paradigm in which task-irrelevant noises occurred. To understand the effects of time on responsiveness, responses recorded during the first and second half of each paradigm were compared. Because N1 and startle blinks tend to decrease over time, task relevance effects are confounded with time effects.

METHOD

Subjects

Fifteen healthy young subjects (8 men and 7 women; 19–25 years, mean = 21.7 years, SD = 2.02), 11 healthy elderly subjects (5 men and 6 women; 58–76 years, mean = 66.5 years, SD = 5.87), and 12 patients with probable Alzheimer's Disease (8 men and 4 women; 59–77 years, mean = 68.7 years, SD = 4.92) participated. The age difference between the elderly and AD subjects was not significant. Average education levels were 14.2 years for the young (13–17 years, SD = 1.27), 14.8 years for the elderly (12–18 years, SD = 2.5), and 13.8 years for the AD patients (5–19 years, SD = 3.6). Education differences among the groups were not significant. Mini-Mental State scores (6) were 29.3 for the young (28–30, SD = 0.18), 28.2 for the elderly (26–30, SD = 1.25), and 20.3 for the AD patients (13–25, SD = 1.04). Groups were tested with standard audiologic exams. Subjects with hearing losses greater than 35 dB at 1,000 Hz in both ears were excluded. All subjects gave informed consent.

Controls

Healthy controls were recruited and screened by telephone interview and questionnaire to exclude those with a history of significant psychiatric or neurological disease, recent use of psychoactive drugs or other drugs with significant central nervous system (CNS) effects, or alcohol consumption exceeding 50 g/day for a month or more. One elderly control included in the analysis had been taking subtherapeutic doses of the tricyclic antidepressant, nortriptyline, although she believed it was not for depression.

Patients

The AD subjects were drawn from a pool of patients evaluated at the Geriatric Psychiatry Research Unit and NIMH Dementia Clinical Research Center of the Palo Alto VA Health Care System. The patients included in this analysis met the NINCDS-ADRDA criteria for probable AD. Because many of these patients have been followed longitudinally, they were classified for the present study according to their most recent diagnoses. One patient was excluded from the analysis when his diagnosis changed from AD to dementia associated with Parkinson's Disease and Lewy bodies. Updated diagnoses resulted in all 12 patients being classified as probable. Patients with diagnosable neurological disorders, other than AD, or acute medical conditions were excluded. One AD subject included in the analysis had been taking subtherapeutic doses of the tricyclic antidepressant, nortriptyline, but like the elderly control, she believed it was not for depression. The elderly controls and AD subjects used similar medications including estrogen replacement therapy, diuretics, antihypertensives, nonsteroidal antiflammatory drugs, and angina medications. Although none of the medications was considered to have major CNS side effects, some CNS side effects may have been present.

ERP Testing

ERPs were collected during three paradigms involving noises and tones, in the fixed order listed below. A visual paradigm was presented between the last two paradigms but the visual data are not reported here. Subjects wore earphones and sat upright in a easy chair in a sound attenuated room. Each paradigm took 10.3 min to present. Breaks of 5 to 10 min were taken between paradigms as needed.

Irrelevant Noise Paradigm. Subjects were presented with a series of 320 tones and 80 noises with a fixed interstimulus interval of 1.5 s. The tones were 500 Hz, 70 dB SPL (A scale), 50 ms duration and occurred on 80% of the trials. The noises were broad band, 105 dB SPL, 50 ms duration and occurred on 20% of the trials. Tones had a shaped rise and fall time of 5 ms. Noises rose and fell in 4–5 ms because of the response characteristics of the earphones, although input to the amplifiers rose and fell in 100 μs. Stimuli were presented in a Bernoulli sequence held constant across subjects. Subjects were given written and verbal instructions simply to relax and listen.

Relevant Tone Paradigm. Stimulus sequence parameters were identical to the Irrelevant Noise paradigm, except that the noise was replaced by a 1000 Hz, 70 dB SPL, 50 ms duration tone. Subjects were asked to press a reaction time (RT) button to the 1000 Hz relevant tones, giving equal importance to speed and accuracy. (Two subjects—one elderly and one AD—had excessive movement artifacts in this paradigm and could not be used in analyses involving this paradigm.)

Relevant Noise Paradigm. Stimulus sequence parameters were identical to the Irrelevant Noise paradigm. In this paradigm, subjects were asked to press an RT button to the relevant noises, giving equal importance to speed and accuracy. Thus, this paradigm differs from the Irrelevant Noise Paradigm only in that the noises are targets, and it differs from the Relevant Tone Paradigm in that the targets are loud and noises.

EEG and EOG Recording

Electroencephalograms (EEG) were recorded from the 19 standard 10–20 sites. A sterno-vertebral reference with a balancing circuit was used to minimize electrocardiogram (EKG) artifacts (50). Technical difficulties with Oz and FPz electrodes in many of the subjects necessitated eliminating those waveforms from the data analysis, leaving data from 17 scalp electrode sites and two eye derivations for analysis. Vertical electro-oculograms (EOG) were recorded from electrodes placed above and below the right eye, and horizontal EOG from electrodes placed at the outer canthus of each eye. EEG and EOG were sampled every 5 ms for 1,250 ms, beginning 100 ms before stimulus onset. A microcomputer-controlled Nihon-Kohden EEG-4221 system (Tokyo, Japan) recorded EEG at a gain of 10 K and EOG at 2.7 K with a bandpass of 0.13–70 Hz.

ERP Data Screening. Single trials were individually screened by computer algorithm before being included in the signal averages. First, trials on which button press errors occurred or on which EEG at any electrode site saturated the A/D converter ($> \pm 250$ μV) were rejected. Next, single trials at each electrode were individually corrected for the effects of eye blinks and eye movements using the procedure of Gratton et al. (15) as refined by Miller et al. (25). This method was chosen by Perlstein et al. (31) to study reflex blinks and ERPs, and its validity is equal to that of its alternatives (1). Finally, after a baseline was established, trials with movement or electrical artifacts (voltages $> \pm 200$ μV from baseline) were rejected. ERP averages were derived from responses to the rare and background stimuli from each paradigm. Before peak identification, EEG was filtered with a 0.5 Hz (down 3 dB) highpass filter (2) and a 12.4 Hz (down 3 dB) lowpass filter (46).

ERP Component Identification and Assessment. N1 was measured at Cz as the most negative point between 50–150 ms, and P300 was measured at Pz as the most positive point between 275–600 ms. These electrode sites were chosen because the peak amplitudes are usually largest there. N1 was measured to both the rare and background events in each paradigm; P300 was measured only to the rare event. To assess the scalp distribution of P300, P300 amplitude was measured across a grid of 15 electrode sites at the latency of P300 at Pz. This allowed analysis of three coronal rows from the five electrodes at each of the frontal (F7, F3, Fz, F4, F8), central (T3, C3, Cz, C4, T4), and parietal (T5, P3, Pz, P4, T6) locations, as well as five sagittal rows from three electrodes each at the far left (F7, T3, T5), midleft (F3, C3, P3), midline (Fz, Cz, Pz), midright (F4, C4, P4), and far right (F8, T4, T6) locations. To assess distributional differences across groups, time, and paradigms, independent of group and paradigm differences in amplitude, P300 amplitudes at these electrode sites were normalized, within each group and both halves of each paradigm, according to the equation of McCarthy and Wood (24):

$$\mathrm{P300}(i') = [\mathrm{P300}(i) - \mathrm{P300}(\min)]/[\mathrm{P300}(\max) - \mathrm{P300}(\min)]$$

where i = a given electrode site and i' = the normalized value, and where min = within-group minimum value of 15 electrode sites and max = within-group maximum value of 15 electrode sites for both halves of each paradigm. This resulted in the repeated factors of left-to-right (L/R) (five levels) and anterior/posterior (A/P) (three levels).

Startle Blink Identification. Single-trial VEOG was filtered with a lowpass of 20.7 Hz (down 3 dB) (46). Single-trial VEOG excursions exceeding $+100$ μV were counted as blinks. Startle blinks were defined as those occurring between 50 and 250 ms following the noises.

Statistical Analysis

Two sets of repeated-measures analyses of variance (ANOVAs) were done on the experimental effects. In one, the effect of task relevance was analyzed (relevant noise vs. irrelevant noise). In the other, the effect of intrusiveness was analyzed (relevant noise vs. relevant tone). In both sets, the effect of subject group (young, elderly, AD) was analyzed. When a significant effect of group was obtained, post hoc *t*-tests were performed to establish the significance of age (young vs. elderly) and disease (elderly controls vs. Alzheimer's disease patients). When a significant interaction with group was obtained, post hoc analyses were performed looking for the effect of the variable for each group, as well as looking for the effect of group within both levels of the variable. If there was a significant effect of group at any level of a variable, *t*-tests were made to establish whether the group effect was due to the effects of age or disease.

To evaluate response decrement during a paradigm, responses recorded during the first and second halves of each paradigm were compared for the repeated factor of time and the interaction of group and time. The main effect of group was investigated as part of the above analyses.

Peak amplitudes, latencies, and blink counts were the dependent variables in each of the above ANOVAs. In the Intrusiveness analyses, RTs and errors of omission to relevant noise and relevant tone, and false alarms to background tones, were compared across groups and conditions. The statistical results are presented in the tables, and are not duplicated in the Results section.

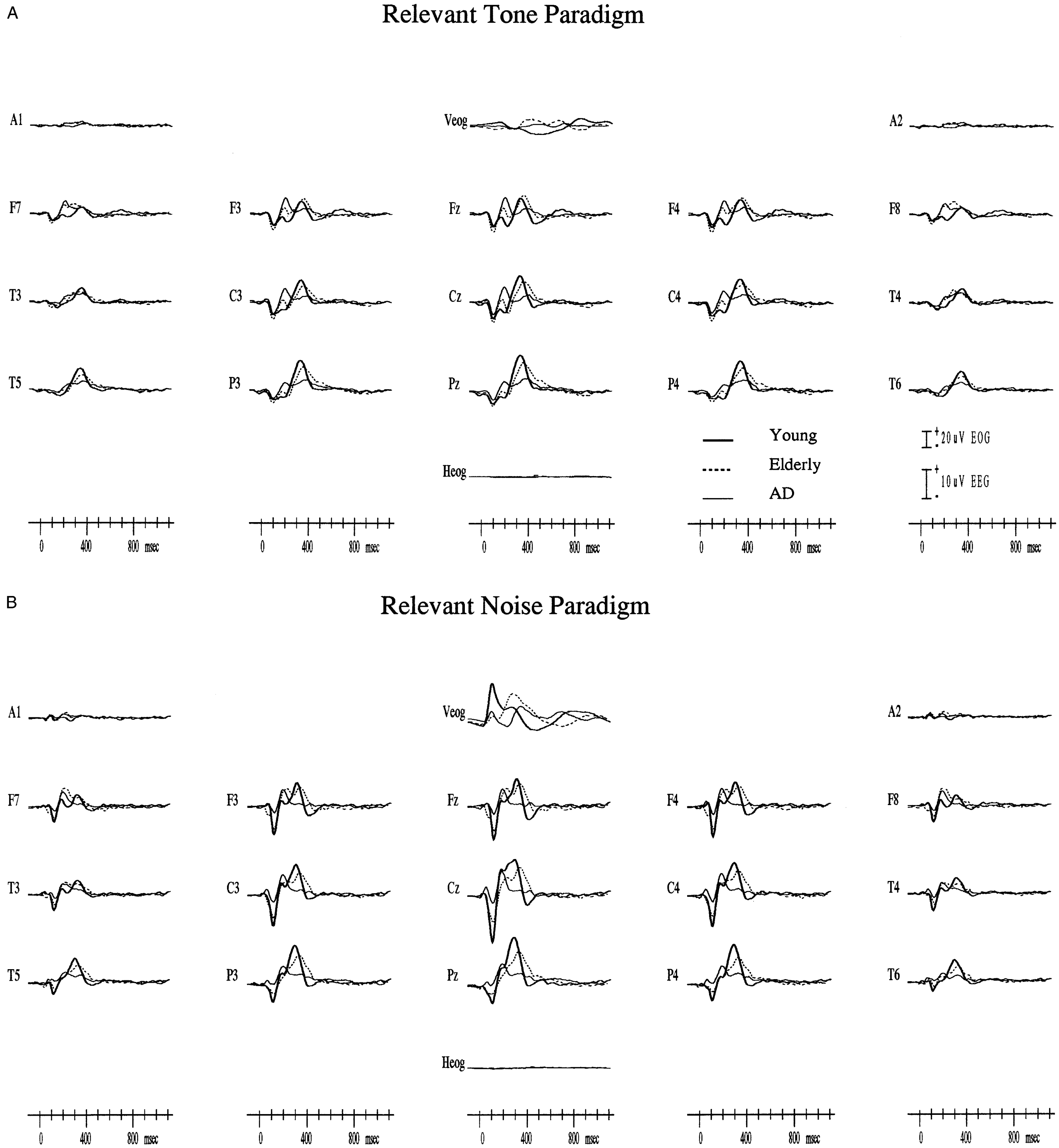
The normalized P300 amplitudes were analyzed in an ANOVA for the repeated factors of intrusiveness, task relevance, time, and left-to-right (L/R) (far left, left, middle, right, far right) and anterior/posterior (A/P) (frontal, central, parietal) scalp distributions.

Greenhouse-Geisser corrections for repeated measures were used whenever appropriate.

RESULTS

Intrusiveness: Relevant Noises vs. Relevant Tones

The grand averages for the three groups for this comparison appear in Fig. 1A and B. N1 amplitude was affected by a significant interaction of group and intrusiveness (Table 1). As can be



seen in Fig. 2, N1 was significantly larger to the relevant noise than to the relevant tone, but the effect was only significant in young and elderly controls, with a trend for AD patients. To the noise, young had larger N1 responses than did elderly; this was not true for the tone. To the tone, elderly controls had larger N1s than did AD patients; this was not true for the noise. The latency of N1 was not affected by any of the variables (Table 1).

Like N1 amplitude, P300 amplitude was affected by an interaction of group and intrusiveness (Table 1). As can be seen in Fig. 2, in young subjects, the noise elicited a larger P300 than did the tone. Intrusiveness had little effect on the P300 amplitude of older controls and AD patients. To the tone, there were significant effects of age and disease, with younger controls having larger P300s than older controls who had larger P300s than AD patients. The same pattern was seen to the noise. P300 latency was shorter to the noise than to the tone, as can be seen in Fig. 3. It was also

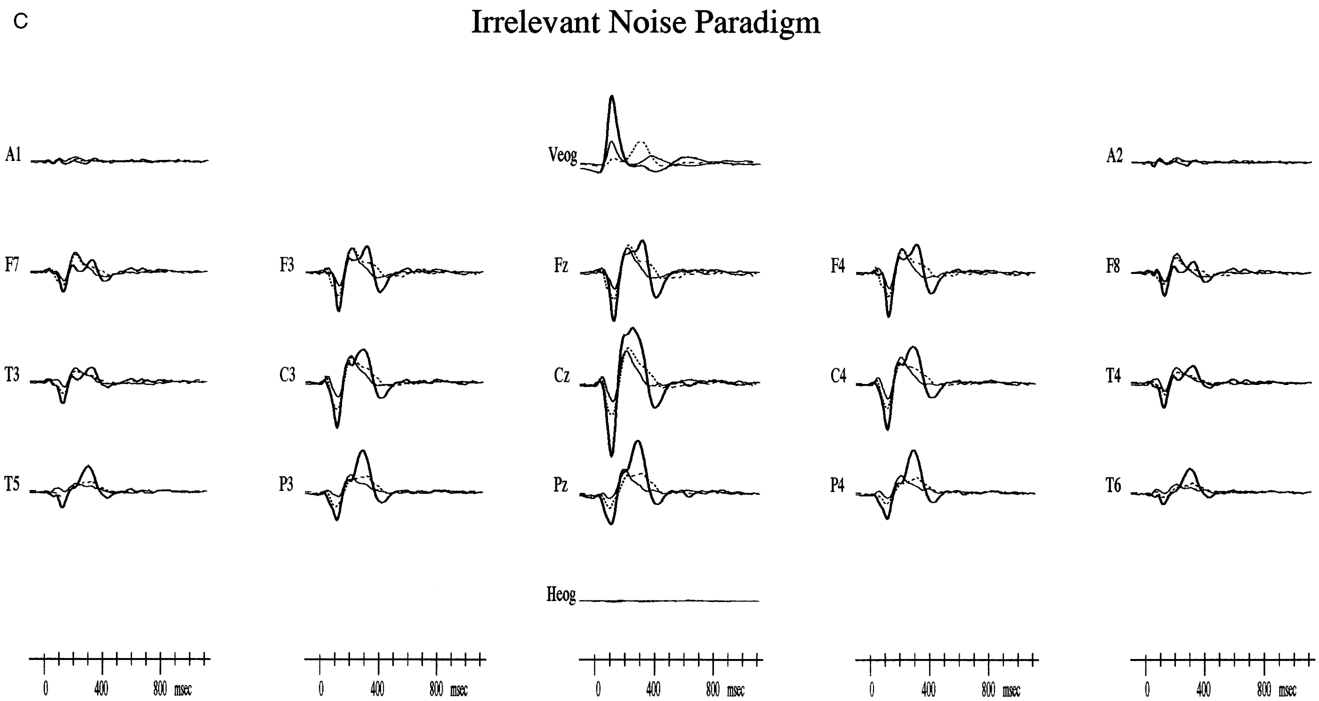


FIG. 1. Grand average ERPs for the three groups the are overlaid for the Relevant Tone paradigm (A), the Relevant Noise paradigm (B), and the Irrelevant Noise paradigm (C). VEOG activity has been mathematically removed from the ERPs but is shown here for illustrative purposes. Scalp positivity is plotted up.

shorter in older controls than in AD subjects, but was not shorter in younger than in older controls (Table 1).

The scalp distributions of P300 to the relevant tone and relevant noise were not different, as can be seen in Fig. 4 and Table 2. Also, distributions did not change with time, nor did time interact significantly with the other variables. The anterior/posterior (A/P) scalp distribution of P300 did not depend on group, as can be seen in Table 2 by the lack of significant effects involving group. Because of a precedence in the literature for a flatter midline A/P distribution in older compared to younger subjects (9,11), data

TABLE 1

INTRUSIVENESS: RELEVANT NOISES VS. RELEVANT TONES

Variable	Group $df = 2, 33$		Intrusiveness $df = 1, 33$		GX I $df = 2, 33$		Post Hoc Tests All Inequalities, $p < 0.05$
	F	p	F	p	F	p	
N1 Amplitude at Cz	7.10	0.003	27.7	0.0001	6.77	0.004	Y: Noise > Tone* O: Noise > Tone Noise: Y > O = AD† Tone: Y = O > AD
N1 Latency at Cz	0.46	NS	2.14	NS	0.68	NS	
P300 Amplitude at Pz	20.6	0.0001	4.62	0.04	5.14	0.02	Y: Noise > Tone Noise: Y > O > AD Tone: Y > O > AD
P300 Latency at Pz	9.09	0.0007	6.71	0.02	0.02	NS	Group: Y = O < AD Intrusiveness: Tone > Noise
RTs	8.03	0.001	12.8	0.001	1.15	NS	Group: Y = O < AD Intrusiveness: Noise < Tone
Misses	4.25	0.03	0.20	NS	0.18	NS	Group: Y = O < AD
False alarms	4.05	0.03	5.64	0.03	0.82	NS	Group: Y < AD Intrusiveness: Noise < Tone

* In this and subsequent tables, Y = Young, O = Old, AD = Alzheimer's Disease.

† In this and subsequent tables, equalities are not used in their mathematical sense but merely to indicate the lack of significant difference.

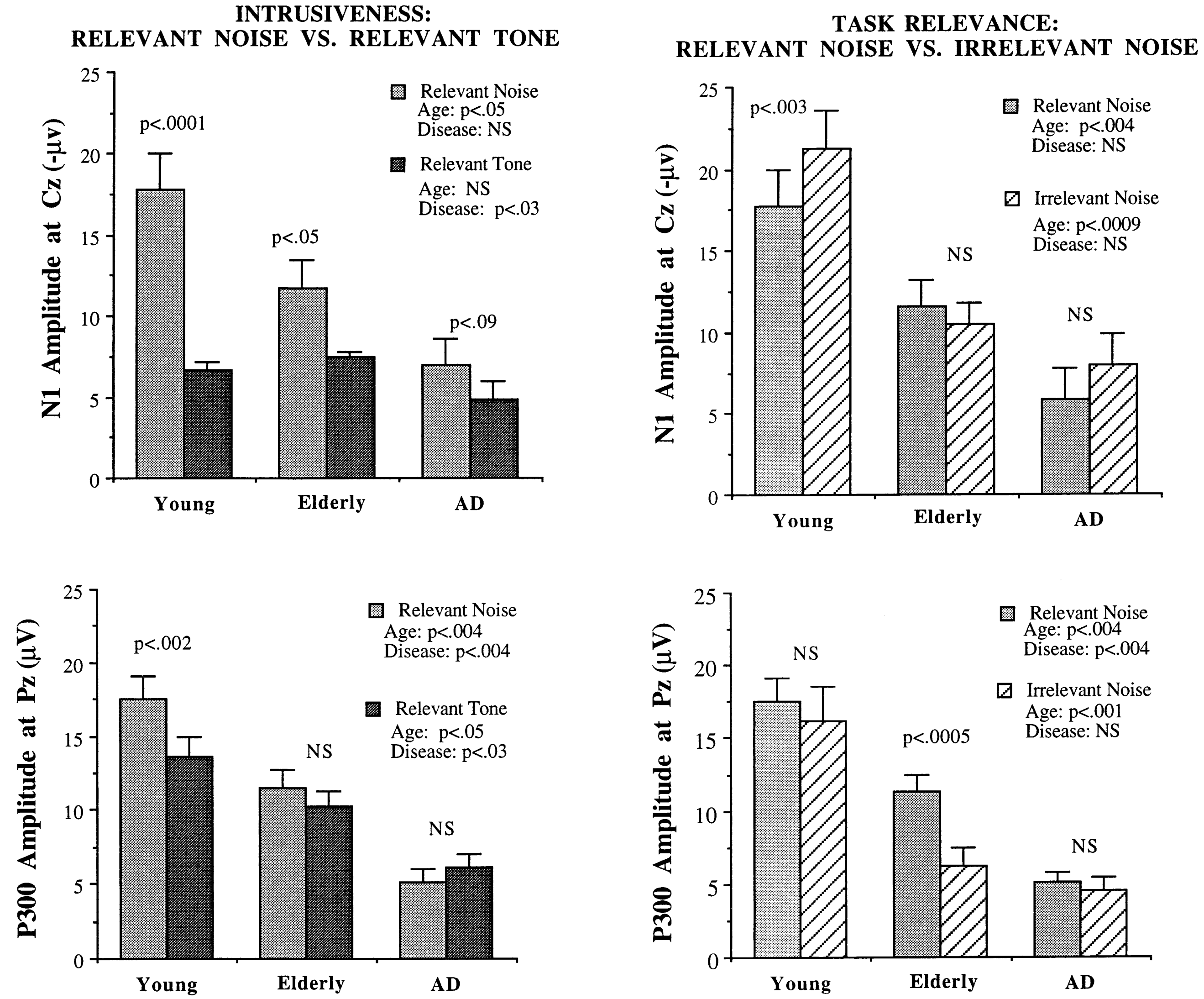


FIG. 2. The effect of Intrusiveness (left) and Task Relevance (right) on N1 (top) and P300 (bottom) amplitudes for the three groups. In all figures, bars reflect standard error of the mean.

from Fz, Cz, and Pz for younger and elderly subjects were compared and a significant group × A/P interaction ($p = 0.05$) was found.

Reaction times to the targets were faster when the target was a noise than when it was a tone (Table 1 and Fig. 3). Although misses were not affected by intrusiveness, false alarms were, with more false alarms being made to background tones when tones were targets than when noises were. Also, young and elderly subjects responded faster than AD subjects. AD subjects missed more targets than did young or elderly controls and committed more false alarms than did the young (Table 1 and Fig. 3).

Mean amplitudes of N1 to background tones are graphed in Fig. 3 where it can be seen that the presence of a loud noise in the paradigm did not affect N1 amplitude of the background tones. Although N1 to the background tones in these two paradigms tended to be larger in the elderly, the effect of age for this comparison was not significant. N1 latency to background tones was not affected by any of the variables.

Task Relevance: Relevant vs. Irrelevant Noises

The grand averages for the three groups for this comparison appear in Fig. 1B and C. In these comparisons, the critical variable is whether or not the noise is a target. Because of interactions of group and relevance (Table 3), the effects of each must be discussed with regard to the other. As can be seen in the top of Fig. 2, N1 was smaller when the noise was relevant (in the paradigm presented third) than when it was irrelevant (in the paradigm presented first), but this only occurred in young control subjects. (This effect may be due to response decrement over time, as described below.) N1 was smaller in older than in younger controls for both the relevant and irrelevant noises. Disease tended to further reduce N1 to the relevant noise ($p = 0.06$). As can be seen in Table 3, the latency of N1 was not affected by any of the variables.

P300 amplitude was also affected by an interaction of group

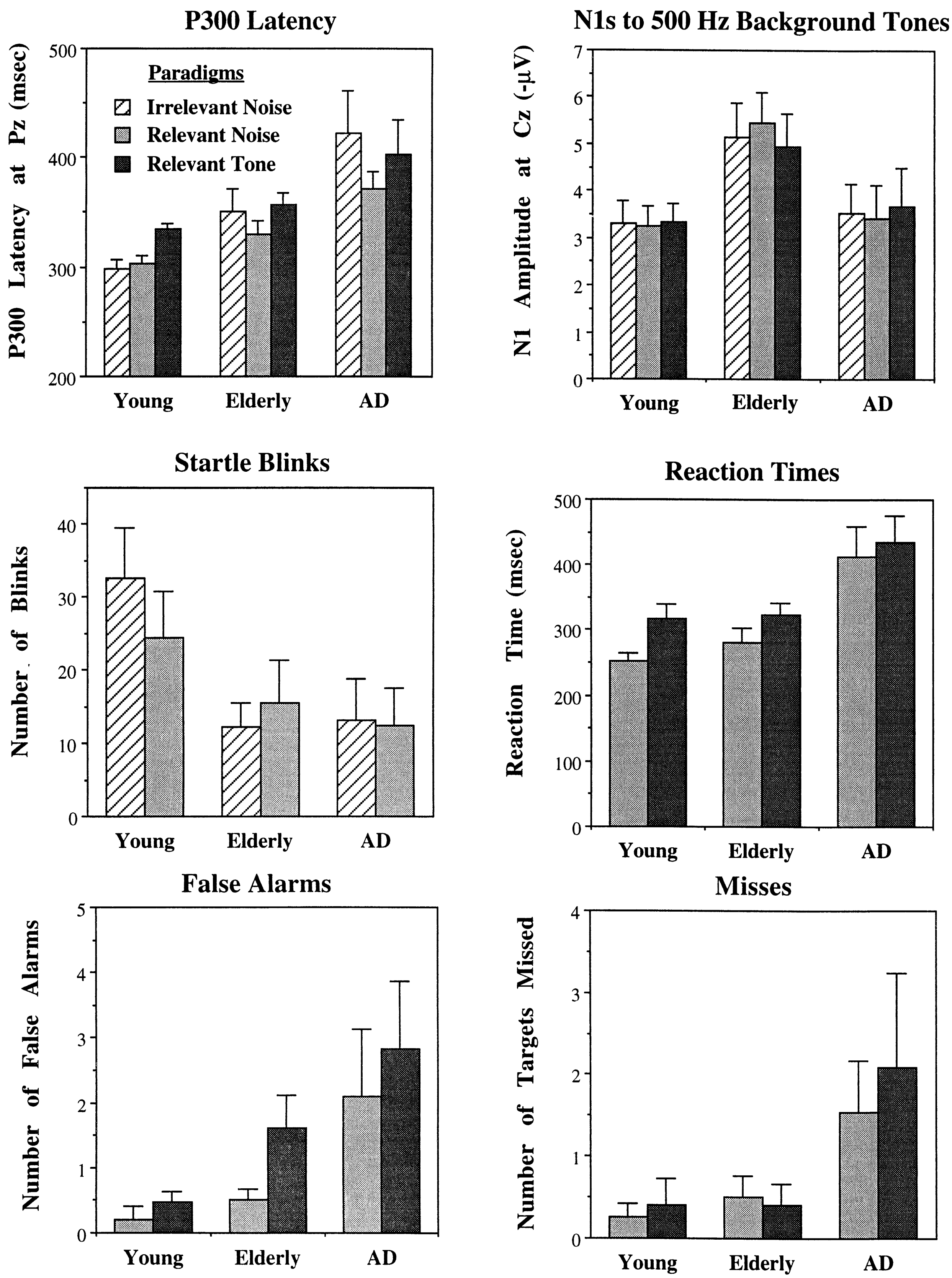


FIG. 3. P300 latencies to rare events, N1 amplitudes to the background tones, Startle Blinks to noises, RTs to rare events, False Alarms to background tones, and Missed rare events are plotted for each paradigm in which they were collected.

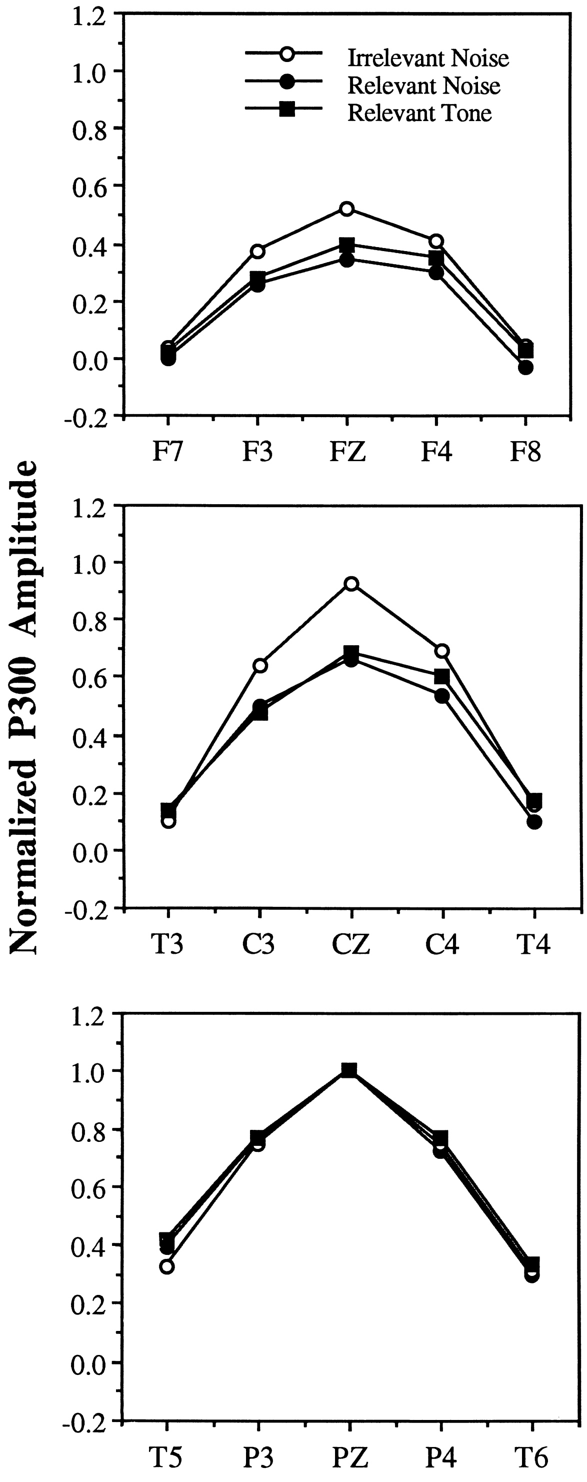


FIG. 4. Normalized P300 amplitudes are compared for the three paradigms at the frontal, central, and parietal electrode sites for the three groups averaged together.

and relevance (Table 3). As can be seen in the bottom of Fig. 2, in older controls, P300 was significantly larger to the relevant than to the irrelevant noise; this was not true for AD patients or young controls. Also, regardless of whether the noise was relevant or not, P300 was smaller in elderly than in young controls. To the relevant noise, P300 was still smaller in AD patients than in older controls. P300 latency was longer in AD patients than in older controls, but not significantly longer in older than younger controls. Task relevance of the noise had no effect on the latency of P300 (Table 3).

The anterior/posterior (A/P) and left-to-right (L/R) distribution of P300 depended on whether the noise was relevant, as can be seen in Fig. 4 and Table 2. To the relevant noise, P300 had a more extreme A/P distribution, being relatively smaller at frontal and central sites than at parietal sites; to the irrelevant noise, P300 was more centrally distributed. Also, P300 distributions were not affected by time, and time did not interact significantly with the other variables.

As is apparent in Fig. 3 and Table 3, there were more startle blinks to irrelevant than to relevant noises, but only in young subjects. Again, this effect may be due to response decrement over time, as described below. To the irrelevant noise, young subjects startle blinked more often than did the older controls. To the relevant noise, there was no difference among the groups.

Whether N1 to the background tones was affected by the relevance of the noise and whether it was affected by group were both investigated by comparing N1s across paradigms and groups (Fig. 3). N1 to the background tones was larger ($p < 0.05$) and earlier in the elderly ($p < 0.05$). It was not affected by whether subjects were performing a task.

Response Decrement over Time Within a Paradigm

Table 4 presents the results of the analyses comparing the responses in the first and second halves of each paradigm. N1 amplitude to the noises was significantly smaller during the second half of both paradigms with noises. There was no effect of time on N1 to relevant tones. There was no differential decrement in N1 for the different groups during any of the paradigms. P300 amplitude and latency were not affected by time in any paradigm, nor was there a differential effect of time for the different groups in any paradigm. Blink counts diminished by the second half of the paradigm, but only significantly during the first paradigm when the noise was irrelevant. The decrement was significant for the young and AD subjects, but not for the elderly.

TABLE 2

SCALP DISTRIBUTION OF NORMALIZED P300 AMPLITUDES

Variable	*F*-Ratio	*df*	*p*
Relevant Noises vs. Relevant Tones			
Analysis of Variance factors: Intrusiveness, Group, Time, L/R, A/P			
L/R (left/right)	100.0	4, 132	0.0001
A/P (anterior/posterior)	42.7	2, 66	0.0001
L/R × A/P	11.9	8, 264	0.0001
Relevant Noises vs. Irrelevant Noises			
Analysis of Variance factors: Task relevance, Group, Time, L/R, A/P			
L/R (left/right)	83.4	4, 410	0.0001
A/P (anterior/posterior)	47.1	2, 70	0.0001
Task relevance × L/R	3.60	4, 410	0.04
Task relevance × A/P	2.74	2, 70	0.10
L/R × A/P	10.1	8, 280	0.0001
Task relevance × L/R × A/P	5.15	8, 280	0.0008

Only effects significant at $p \leq 0.10$, after Greenhouse-Geisser correction, are listed.

TABLE 3

TASK RELEVANCE: RELEVANT NOISES VS. IRRELEVANT NOISES

Variable	Group $df = 2, 33$		Relevance $df = 1, 33$		Group × Relevance $df = 2, 33$		Post Hoc Tests All Inequalities, $p < 0.05$
	F	p	F	p	F	p	
N1 Amplitude at Cz	11.9	0.0001	6.32	0.02	4.97	0.02	Y: NT > T Relevant: Y > O = AD Irrelevant: Y > O = AD
N1 latency at Cz	0.07	NS	1.68	NS	0.96	NS	
P300 amplitude at Pz	20.1	0.0001	11.1	0.002	3.88	0.03	O: T > NT Relevant: Y > O > AD Irrelevant: Y > O = AD
P300 latency at Pz	11.2	0.0002	1.21	NS	0.61	NS	Y = O < AD
Startle blink counts	2.64	NS	1.25	NS	3.68	0.04	Y: NT > T Irrelevant: Y > O = AD

DISCUSSION

First, data are discussed in terms of experimental effects and then summarized in terms of group effects.

Stimulus Intrusiveness

The effects of intrusiveness were investigated by comparing responses to target events when they were startling noises and moderate tones. Because a button press was required, effortful attention was being allocated in both situations, but in one case the stimulus was intrusive and in the other it was not. Noises elicited significantly larger P300s than tones but only in young subjects, the difference being almost 4 μV. However, noises elicited significantly larger N1s in both young and elderly subjects, the difference being more than 10 μV in young, and more than 4 μV in elderly. Although N1 was sensitive to the difference between tones and noises in the elderly, P300 amplitude was not.

In all groups, noises elicited shorter latency P300s and faster RTs than tones. Roth et al. (44), like many others, found that RTs are faster to louder noises, perhaps due to a general increase in arousal or activation. It is interesting that any noise-induced effects

TABLE 4

RESPONSE DECREMENT OVER TIME: FIRST HALF VS. SECOND HALF

Irrelevant Noise Paradigm					
Variable	Time $df = 1, 35$ F	Time p	Group × Time $df = 2, 35$ F	Group × Time p	Post Hoc Tests All Inequalities, $p < 0.05$
N1 Amplitude at Cz	18.1	0.0002	1.85	NS	1st > 2nd
P300 Amplitude at Pz	1.64	NS	0.12	NS	
P300 Latency at Pz	0.44	NS	0.52	NS	
Blink counts	12.7	0.001	6.50	0.004	Y: 1st > 2nd AD: 1st > 2nd 1st: Y > O = AD

Relevant Tone Paradigm				
Variable	Time $df = 1, 33$ F	Time p	Group × Time $df = 2, 33$ F	Group × Time p
N1 Amplitude at Cz	0.40	NS	0.47	NS
P300 Amplitude at Pz	0.29	NS	0.35	NS
P300 Latency at Pz	2.17	NS	0.29	NS

Relevant Noise Paradigm				
Variable	Time $df = 1, 35$ F	Time p	Group × Time $df = 2, 35$ F	Group × Time p
N1 Amplitude at Cz	2.81	NS	1.81	NS
P300 Amplitude at Pz	0.01	NS	1.51	NS
P300 Latency at Pz	1.18	NS	0.80	NS
Blink counts	3.76	0.06	1.67	NS

of arousal or activation were the same in young, elderly, and AD subjects. This represents another divergence from the P300 amplitude data, which suggested a relative insensitivity to intrusiveness in elderly and AD subjects.

Task difficulty differences may also have been responsible for intrusiveness effects on P300 latency and RT. Behavioral data suggest that accurate responding to the tone was more difficult than to the noise. Although the numbers of missed targets were not greater, there were more false alarms when a tone was the target. This discrimination difficulty may have been reflected in longer latency P300s and slower RTs to the relevant tones.

This relative insensitivity of P300 amplitude in the elderly to noises confirms previous results (9,10). In the latter report, an attempt was made to rule out age-related sensory explanations for the insensitivity of P300 to noises. To this end, the bandwidth was narrowed to 0–1,000 Hz and noise intensities set relative to each subject's threshold. Still, no enhancement of noise-elicited P300 was seen in the elderly.

Task Relevance

The effects of task relevance were investigated by comparing responses to noises in paradigms where they were task relevant and irrelevant. In both paradigms, attention was automatically elicited by the loud noises as evidenced by the presence of the P300 component (41,42). By making the noise task relevant, effortful attentional processes were added to the existing automatic ones. As expected, task relevance added significantly (5.1 μV) to the automatic P300 in elderly subjects, but counter to expectation, it did not add significantly in AD subjects.

Earlier, an exaggerated age-related reduction of P300 to startling noises compared to tones was reported (9,10) but in those studies noises were never task relevant. Kok and Zeef (22) suggested that elderly show less activation than young, resulting in less cortical negativity, which was even further reduced with lower demand tasks. P300 has been postulated to reflect an interruption in cortical negativity with less prestimulus negativity leading to smaller P300s (4,45), perhaps explaining why P300s are smaller in the elderly. According to Kok and Zeef, increasing task demands by adding a button-press requirement should increase cortical activation, thereby increasing P300 amplitude. Indeed, as reported here, age-related reduction in P300 amplitude to noises was smaller when the noise was a target. The addition of the task did not affect P300 amplitude in young subjects, explicable by their already being at maximal levels of activation. Note, tonic differences in cortical activation as an explanatory concept for these aging effects is an alternative to more specific attentional explanations.

Hirst and Volpe (18) found that automatic spatial encoding of information in amnesics improved with instruction but performance of normal controls was not affected. This pattern is similar to that reported here for P300 amplitude to noises. Based on data from cognitively impaired patient groups, Strauss et al. (51) suggested that if automatic processes are impaired, events normally encoded automatically may be encoded with effort, if sufficient capacity is available. The data suggest that in the elderly, sufficient capacity was available. Like the elderly, AD patients demonstrated an automatic processing deficit, but unlike the elderly, AD patients did not have or did not rally the resources to process the noises effortfully. It is important, however, to note that the relevant noise paradigm was presented last, and if AD subjects tire more quickly than healthy elderly, fatigue may be the basis of this apparent insufficiency.

To the extent that P300 latency is a metric of stimulus evaluation time, independent of response processing (23), it is safe to say that the noises were evaluated with equivalent speed regardless of whether they were task relevant. This lack of effect was seen for all three groups, suggesting that when elicited by noises, P300 latency is unaffected by response requirements similarly in all groups.

Task relevance has been shown to increase the amplitude of both N1 (16,26) and P300 (19). For both components, task relevance directs attention to the stimuli, and attention increases the amplitudes. Surprisingly, for young subjects, N1 was smaller to relevant than irrelevant noises. This could be a time effect since N1 decreased with time, as shown before (12), and irrelevant noises were presented before relevant noises. The effects of time between paradigms cannot be extrapolated perfectly from the effects of time within a paradigm, but if the effects of time are apparent within a paradigm, it is likely that they will be significant over longer time periods as well. The effects of task relevance on P300 are probably not due to time effects because P300 amplitude did not significantly decrement over time within a paradigm, consistent with previous data (44).

Blink count was also smaller to the task-relevant noise, perhaps due to the effects of time. Although the numbers of blinks in older controls and AD patients were very small, the numbers still fell in the AD patients from the first to the second half of the paradigm, suggesting the absence of a floor effect on this measure. Thus, AD subjects habituate more like young than elderly subjects. Because this is a single, unexpected result, conclusions should not be drawn until it is replicated.

N1 to background tones was remarkably insensitive to the rare stimulus. Task relevance and intrusiveness of the rare stimulus affected the N1 to the background tones by less than ±0.2 μV.

Scalp Distribution of P300

The scalp distribution of P300 depended on task relevance: P300 to the relevant noise had a more parietal distribution while P300 to irrelevant noise had a more central distribution. This is reminiscent of the distributional difference seen between go and nogo stimuli (33), with a go stimulus having a more parietal distribution. Interestingly, the irrelevant noises did not elicit a frontally distributed P3a-like response (21) seen to novel auditory stimuli. The scalp distribution of P300 was not affected by intrusiveness, being the same for relevant tones and relevant noises. Also, the scalp distribution of P300 did not change with time.

There was a relative lack of a group effect on the anterior/posterior scalp distribution of P300 when lateral electrodes were included in the analysis. When only central midline electrodes were considered, a flatter distribution was seen in the elderly, replicating a large literature (8,11,35,38).

Scalp distribution is a criterion often used to establish separateness or uniqueness of components. If this criterion alone were used, and if P300 were distributed differently in young and elderly subjects, then across-group comparisons could not be made. It might be argued, however, that age-related changes in cortical tissue volume (36) could change the distribution of P300 but not the basic nature of the response.

Age and Dementia

As discussed above, the effects of age and disease on P300 amplitude depended on how P300 was elicited. The effortfully elicited P300 was reduced in the elderly as expected (38), and was further reduced with dementia. The automatically elicited P300 was reduced in the elderly as expected (9,10), but contrary to expectation, was not further reduced with dementia. AD patients are not more deficient in automatic processing than elderly controls; their responses to the task irrelevant noises were not different from those of the elderly controls. On the other hand, responses of AD subjects to relevant tones and noises were significantly reduced compared to those of the elderly. P300 amplitude data further suggest that the elderly used effortful resources to process stimuli that are normally processed automatically, while AD patients did not.

The effects of age and dementia on N1 depended on whether N1 was elicited by a rare or background event. As reported earlier (39), age- and dementia-related N1 amplitude deficits appeared only to rare events. Reported here, regardless of task relevance, N1 to noises was reduced with age, but not further with dementia. To relevant tones, N1 was not reduced with age, but was by dementia. To background tones, N1 was largest in the elderly, but equivalent in young and AD subjects. This pattern implies an age-related attention deficit even when attention is elicited automatically, and a dementia-related deficit when attention is effortful. The lack of N1 deficit to background tones suggests sensory processing of these stimuli is intact in both elderly and AD subjects.

As expected, P300 latency was delayed with disease (13,14, 34,37,38), but contrary to expectation, it was not significantly delayed with age. The average age-related delay in P300 latency was only about 25 ms, falling short of the expected 1+ ms/year (32). Although P300 latency is a relative index of stimulus evaluation time within an individual, it is not clear what conclusions can be drawn about P300 latency differences across individuals. Nevertheless, one interpretation of the lack of age-related slowing in P300 is that this sample of elderly was faster than expected at stimulus evaluation.

Contrary to expectation, the significant dementia-related delay in P300 was not reduced by intrusiveness or task relevance. Thus, P300 slowing was not overcome by the arousing quality of the noises or by effort, suggesting that P300 slowing in AD is not due to underarousal or lack of motivation.

Age, but not disease, reduced the numbers of startle blinks to irrelevant noises, confirming other aging findings (9,10) and extending them to AD. Neither age nor disease affected the numbers of startle blinks to the relevant noise.

SUMMARY

In elderly and AD subjects, N1 and P300 amplitudes are differentially sensitive to loud noises. Older people have the sensory ability to appreciate the intensity of loud noises, as reflected in N1 amplitude, but they do not automatically allocate extra resources to them, as reflected in P300 amplitude. In spite of the lack of resources allocated to processing noises, elderly and AD subjects process them more quickly than tones, as reflected in P300 latency and RT data. When asked to make an effortful response to the noises, elderly allocate additional resources, as reflected in P300 amplitude, although young and AD subjects do not. Perhaps young subjects had already allocated a surplus even when not asked to make an effortful response, and AD subjects may have had no more resources available to allocate.

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REFERENCES

1. Brunia, C. H. M.; Mocks, J.; van den Berg-Lenssen, M. M. C. Correcting ocular artifacts in the EEG: A comparison of several methods. J. Gerontol. 40:595–600; 1989.
2. Coppola, R. Isolating low frequency activity in EEG spectrum analysis. Electroencephalogr. Clin. Neurophysiol. 46:224–226; 1979.
3. Donchin, E.; Coles, M. Is the P300 component a manifestation of context updating? (Commentary on Verleger's critique of the context updating model). Behav. Brain Sci. 11:357–374; 1988.
4. Elbert, T.; Rockstroh, B. Threshold regulation—A key to the understanding of the combined dynamics of EEG and event-related potentials. Psychophysiology 1:317–333; 1987.
5. Fisk, A. D.; Rogers, W. A.; Giambra, L. M. Consistent and varied memory/visual search: Is there an interaction between age and response-set effects? J. Gerontol. 45:P81–P87; 1990.
6. Folstein, M. F.; Folstein, S. E.; McHugh, P. R. Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12:189–198; 1975.
7. Ford, J. M.; Duncan-Johnson, C. C.; Pfefferbaum, A.; Kopell, B. S. Expectancy for events in old age: Stimulus sequence effects on P300 and reaction time. J. Gerontol. 37:696–704; 1982.
8. Ford, J. M.; Pfefferbaum, A. Age-related changes in ERPs. In: Ackles, P. K.; Jennings, J. R.; Coles, M. G., eds. Advances in psychophysiology. Greenwich, CT: JAI Press; 1985:301–339.
9. Ford, J. M.; Pfefferbaum, A. Event-related potentials and eyeblink responses in automatic and controlled processing: Effects of age. Electroencephalogr. Clin. Neurophysiol. 78:361–377; 1991.
10. Ford, J. M.; Roth, W. T.; Isaacks, B.; White, P. M.; Hood, S.; Pfefferbaum, A. Elderly men and women are less responsive to startling noises. Biol. Psychol. 39:57–80; 1995.
11. Friedman, D.; Simpson, G.; Hamberger, M. Age-related changes in scalp topography to novel and target stimuli. Psychophysiology 30:383–396; 1993.
12. Fruhstorfer, H. Habituation and dishabituation of the human vertex response. Electroencephalogr. Clin. Neurophysiol. 30:153–161; 1971.
13. Goodin, D.; Squires, K.; Starr, A. Long latency event-related components of the auditory evoked potential in dementia. Brain 101:635–648; 1978.
14. Goodin, D. S. Clinical utility of long latency 'cognitive' event-related potentials (P3): The pros. Electroencephalogr. Clin. Neurophysiol. 76:2–5; 1990.
15. Gratton, G.; Coles, M. G. H.; Donchin, E. A new method for off-line removal of ocular artifact. Electroencephalogr. Clin. Neurophysiol. 55:468–484; 1983.
16. Hansen, J. C.; Hillyard, S. A. Selective attention to multidimensional auditory stimuli. J. Exp. Psychol. 9:1–19; 1983.
17. Hasher, L.; Zacks, R. T. Automatic and effortful processes in memory. J. Exp. Psychol. 108:356–388; 1979.
18. Hirst, W.; Volpe, B. T. Encoding of spatial relations with amnesia. Neuropsychologia 22:631–634; 1984.
19. Johnson, R., Jr. A triarchic model of P300 amplitude. Psychophysiology 23:367–384; 1986.
20. Kahneman, D. Attention and effort. Englewood Cliffs, NJ: Prentice Hall; 1973.
21. Knight, R. T. Decreased response to novel stimuli after prefrontal lesions in man. Electroencephalogr. Clin. Neurophysiol. 59:9–20; 1984.
22. Kok, A.; Zeef, E. J. Arousal and effort: A review and theoretical synthesis of studies of age-related changes in event-related potentials. In: Brunia, C. H. M.; Mulder, G.; Verbaten, M. N., eds. Event-related brain research (EEG Suppl. 42). Amsterdam: Elsevier Science Publishers, B.V.; 1991:324–341.
23. Kutas, M.; McCarthy, G.; Donchin, E. Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. Science 197:792–795; 1977.
24. McCarthy, G.; Wood, C. C. Scalp distribution of event-related potentials: An ambiguity associated with analysis of variance models. Electroencephalogr. Clin. Neurophysiol. 62:203–208; 1985.
25. Miller, G. A.; Gratton, G.; Yee, C. M. Generalized implementation of

an eye movement correction procedure. Psychophysiology 25:241–243; 1988.
26. Näätänen, R. The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. Behav. Brain Sci. 13:201–232; 1990.
27. Näätänen, R.; Picton, T. The N1 wave of the human electric and magnetic response to sound: A review and an analysis of the component structure. Psychophysiology 24:375–425; 1987.
28. O'Donnell, B. F.; Friedman, S.; Squires, N. K.; Maloon, A.; Drachman, D. A.; Swearer, J. M. Active and passive P3 latency in dementia. Neuropsychiatr. Neuropsychol. Behav. Neurol. 3:164–179; 1990.
29. Öhman, A. The orienting response, attention, and learning: An information processing perspective. In: Kimmel, H.; van Olst, E.; Orlebeke, J., eds. The orienting reflex in humans. Hillsdale, NJ: Lawrence Erlbaum Assoc. Inc.; 1979:443–472.
30. Patterson, J.; Michalewski, J. J.; Starr, A. Latency variability of the components of the auditory event-related ptentials to infrequent stimuli in aging, Alzheimer-type dementia and depression. Electroencephalogr. Clin. Neurophysiol. 71:450–460; 1988.
31. Perlstein, W. M.; Fiorito, E.; Simons, R. F.; Graham, F. K. Lead stimulation effects on reflex blinks, exogenous brain potentials, and loudness judgements. Psychophysiology 30:347–358; 1993.
32. Pfefferbaum, A.; Ford, J.; Wenegrat, B.; Roth, W. T.; Kopell, B. S. Clinical application of the P3 component of event-related potentials: I. Normal aging. Electroencephalogr. Clin. Neurophysiol. 59:85–103; 1984.
33. Pfefferbaum, A.; Ford, J. M. ERPs to stimuli requiring response production and inhibition: The effects of age, probability and visual noise. Electroencephalogr. Clin. Neurophysiol. 71:55–63; 1988.
34. Pfefferbaum, A.; Ford, J. M.; Kraemer, H. C. Clinical utility of long latency 'cognitive' event-related potentials (P3): The cons. Electroencephalogr. Clin. Neurophysiol. 76:6–12; 1990.
35. Pfefferbaum, A.; Ford, J. M.; Roth, W. T.; Hopkins, W. F., III; Kopell, B. S. Event-related potential changes in healthy aged females. Electroencephalogr. Clin. Neurophysiol. 46:81–86; 1979.
36. Pfefferbaum, A.; Mathalon, D. H.; Sullivan, E. V.; Rawles, J. M.; Zipursky, R. B.; Lim, K. O. A quantitative magnetic resonance imaging study of changes in brain morphology from infancy to late adulthood. Arch. Neurol. 51:874–887; 1994.
37. Pfefferbaum, A.; Wenegrat, B.; Ford, J.; Roth, W. T.; Kopell, B. S. Clinical application of the P3 component of event-related potentials: II. Dementia, depression and schizophrenia. Electroencephalogr. Clin. Neurophysiol. 59:104–124; 1984.
38. Polich, J. P3 in the evaluation of aging and dementia. In: Brunia, C. H. M.; Mulder, G.; Verbaten, M. N., eds. Event-related brain research. (Electroencephalogr. Clin. Neurophysiol. Suppl. 42). Amsterdam: Elsevier; 1991:304–323.
39. Polich, J.; Ladish, C.; Bloom, F. E. P300 assessment of early Alzheimer's disease. Electroencephalogr. Clin. Neurophysiol. 77: 179–189; 1990.
40. Posner, M. I.; Snyder, C. R. Facilitation and inhibition in the processing of signals. In: Rabbitt, P. M. A.; Dornic, S., eds. Attention and performance—V. London: Academic Press; 1975.
41. Putnam, L. E.; Roth, W. T. Automatic elicitation of cognitive components by startling stimuli. In: Johnson, R., Jr.; Rohrbaugh, J. W.; Parasuraman, R.; eds. Current trends in event-related potential research. Amsterdam: Elsevier; 1987:256–262.
42. Putnam, L. E.; Roth, W. T. Effects of stimulus repetition, duration, and rise time on startle blink and automatically elicited P300. Psychophysiology 27:275–297; 1990.
43. Rohling, M. L.; Ellis, N. R.; Scogin, F. Automatic and effortful memory processes in elderly persons with organic brain pathology. J. Gerontol. 46:P137–P143; 1991.
44. Roth, W. T.; Dorato, K. H.; Kopell, B. S. Intensity and task effects on evoked physiological responses to noise bursts. Psychophysiology 21:466–481; 1984.
45. Roth, W. T.; Ford, J. M. P3 and (de)activation. Behav. Brain Sci. 11:393–394; 1988.
46. Ruchkin, D. S.; Glaser, E. Simple digital filters for examining CNV and P300 on a single-trial basis. In: Otto, D. A., ed. Multidisciplinary perspectives in event-related potential brain research. Washington, DC: U.S. Government Printing Office; 1978:579–581.
47. Salthouse, T.; Babcock, R. L. Decomposing adult age differences in working memory. Dev. Psychol. 5:763–776; 1991.
48. Sanders, R. E.; Gonzalez, E. G.; Murphy, M. D.; Liddle, C. D.; Vitina, J. R. Frequency of occurrence and the criteria for automatic encoding. J. Exp. Psych. Learn. Memory Cogn. 13:241–250; 1987.
49. Schneider, W.; Shiffrin, R. M. Controlled and automatic human information processing I. Detection, search and attention. Psychol. Rev. 84:1–66; 1977.
50. Stephenson, W. A.; Gibbs, F. A. A balanced noncephalic reference electrode. Electroencephalogr. Clin. Neurophysiol. 3:237–240; 1951.
51. Strauss, M. E.; Weingartner, H.; Thompson, K. Remembering words and how often they occurred in memory impaired patients. Memory Cogn. 13:507–510; 1985.
52. Verleger, R. Event-related potentials and cognition: A critique of the context updating hypothesis and an alternative interpretation of P3. Behav. Brain Sci. 11:343–427; 1988.