

COGNITIVE DEFICITS IN CHRONIC ALCOHOLICS AND ELDERLY SUBJECTS ASSESSED BY EVOKED BRAIN POTENTIALS

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It has been hypothesized that alcoholism accelerates the aging process. Most evidence for this hypothesis comes from the neuropsychological literature, where similarities in cognitive functioning between young alcoholics and old people have been reported (*Fitzhugh et al.* 1960, 1965, *Williams et al.* 1973, *Blusewicz et al.* 1977a, b). These neuropsychological studies indicate that alcoholic and geriatric subjects have in common global deficits in abstraction and adaptive abilities, with both groups manifesting perseverative tendencies. However, these neuropsychological techniques must rely solely on behavioral indices. Although alcoholics may exhibit similar behavioral deficits to old people, these behavioral deficits may well reflect the result of different neuronal pathology, or are general enough to be non-specific.

The event-related potential (ERP) technique offers a unique approach for assessing level of brain functioning in that it combines cognition with electrophysiology. ERP's can be recorded to various sensory stimuli in conjunction with behavior (Begleiter 1979). Therefore, the ERP is an ideal technique for assessing similarities in brain functioning between alcoholics and old people.

For the past several years in our laboratory, we have systematically examined electrophysiological aberrations in various patient populations with the use of event-related potential (ERP) techniques. These ERP techniques require the subject to be actively engaged in a task, usually an information-processing task. We have been particularly interested in assessing brain dysfunction in chronic alcoholics who have been abstinent from alcohol for long periods of time. In one recent study (Porjesz & Begleiter 1979) we found that the ERP late component, N1-P2, a component sensitive to the selection of relevant or irrelevant stimulus modality, was markedly reduced in alcoholics to all stimuli regardless of task relevance. These results indicated that alcoholics have difficulty differentiating between relevant and irrelevant inputs.

In the present study, we decided to use a particular event-related potential component that is most sensitive to certain aspects of information processing, namely the P3 or P300 component. The P300 component is a positive occurring deflection, so named because it occurs approximately 300 msec after the stimulus. A P300 wave can only be elicited under rather specific conditions; namely:

1. The subject (S) is actively attending to the stimulus sequence (discriminating targets from non-targets), and a different decision or response is required to the targets (*Sutton et al.* 1965, 1967).

2. The targets *must* occur unpredictably and infrequently (Tueting *et al.* 1971).

Thus the P300 paradigm is ideal to investigate the ability of subjects to differentiate between relevant and irrelevant stimuli, and the ability of subjects to probability-match stimuli in terms of their frequency of occurrence. We conducted a P300 study to examine visual ERP (VERP) characteristics to relevant and irrelevant visuo-spatial stimuli in chronic alcoholics and geriatric subjects in an experiment that required them to change sets; stimuli that were relevant in one block were no longer relevant in another block.

METHODS

Subjects

Three groups of education-matched, right handed male subjects were studied: 30 alcoholics, 10 geriatrics and 30 controls. The alcoholics had been drinking an average of $9\frac{1}{2}$ years and a minimum of 7 years. They had a mean age of 36 and had been abstinent from alcohol for a minimum of $1\frac{1}{2}$ months. Only alcoholics who were otherwise healthy and medication-free for a minimum of 3 weeks were accepted for the study.

The geriatric subjects were healthy, medication-free elderly people who were all over 65 years of age, with a mean age of 72. They ranged from non-drinkers to occasional "social drinkers", and none had ever had a drinking problem.

The control group consisted of medication-free young healthy males who were age-matched to the alcoholic group with a mean age of 34. Their drinking histories were similar to those of the geriatric group.

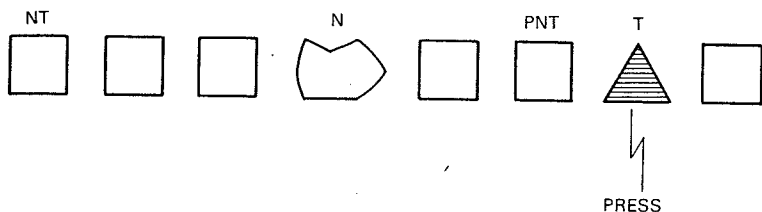
Procedure

The subject was seated in a sound-attenuated room with his head resting on an adjustable chin-rest so that he was looking directly at a computer-generated display located 50 cm from his eyes. He was instructed to fixate in the center of his visual field at all times. All stimuli were presented in the center of the CRT, one at a time, at a random rate of 2–5 seconds apart. The stimuli consisted of two regular geometric shapes (square and triangle), and irregular geometric forms, all equated for size and intensity (Fig. 1).

The S's task was to press a button only to the target stimulus which was either a square or triangle. When the square was the target, the triangle was the non-target and vice-versa, such that ERP's could be obtained to the same stimulus when it served as a target or non-target. The target stimuli occurred rarely, only 8.3 % of the time, as did the novel stimuli (irregular shapes), while the non-targets made up the remaining 83.3 % of the stimuli. Each novel stimulus was presented only once.

EXPERIMENTAL STIMULUS SEQUENCE

BLOCK 1



BLOCK 2

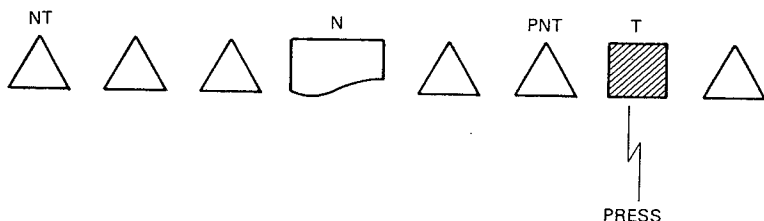


Figure 1. Schematic illustration of representative experimental stimulus sequence indicating frequently occurring Non-Targets (NT), rarely occurring Novels (N) and rarely occurring Targets (T). The S is required to press a microswitch only after the occurrence of the Target. The Non-Targets immediately preceding the Target stimuli that were used for data analysis are labelled "Preceding-Non-Targets" (PNT). The Target and Non-Target stimuli consisted of either a square or triangle such that when the triangle was target the square was non-target; these were alternated every other block. Each Novel stimulus was presented only once.

The target and non-target stimuli were reversed for every block, such that they alternated every other block (e.g. triangle, square, triangle, square or square, triangle, square, triangle). A tone indicated the beginning of a new block, and the S had to keep track of which stimulus was target and which was non-target.

Monopolar recordings were obtained from midline occipital (Oz), parietal (Pz), central (Cz), and frontal (Fz) scalp locations in accordance with the 10-20 International System, using the linked ears as reference and the nasion as ground; vertical eye leads recorded electro-oculogram (EOG) to monitor possible eye-movement contamination.

The ERP's were amplified by Grass amplifiers (bandwidth 0.3-60 hz) and were sampled by a PDP 11/40 computer for a 500 msec epoch (200 pts/sec). A typical ERP waveform is illustrated in Fig. 2. This waveform is the centroid of the control group, obtained by collapsing ERP's over the electrodes and stimulus categories. Peak-to-peak amplitude and latency measures were obtained for peaks P1, N1, P2, N2 and P3. Latency measures were taken as the time of occurrence of these peaks (in msec).

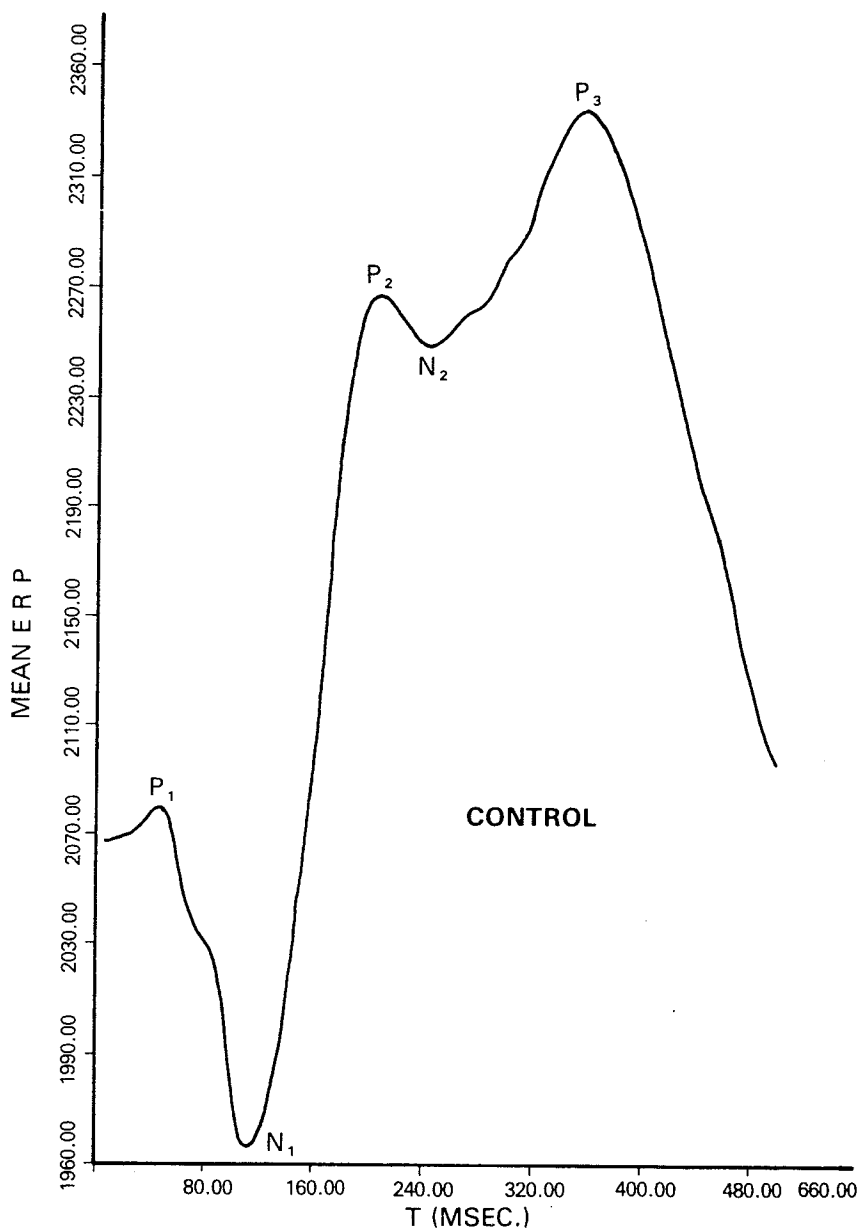
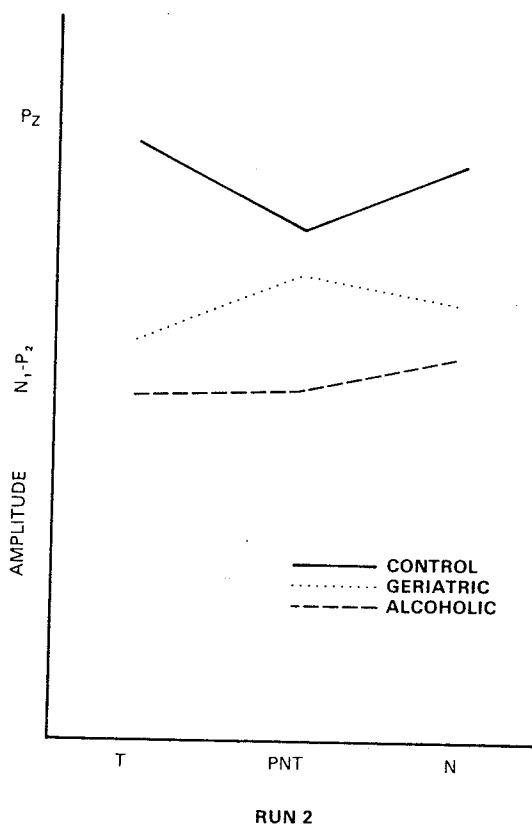


Figure 2. Centroid waveform of ERP's recorded from all control subjects, obtained by collapsing VERP's over midline electrodes (Fz, Cz, Pz and Oz) and over stimulus categories (T, PNT and N), indicating the convention adopted in labelling successive peaks with regard to polarity and ordered according to their time of occurrence as follows: P₁ (50-100), N₁ (100-145), P₂ (150-250), N₂ (200-275) and P₃ (300-500). An amplitude consists of the perpendicular distance between adjacent peaks, as follows: P₁-N₁, N₁-P₂, P₂-N₂ and N₂-P₃.

In order to do the data analysis on an equal number of ERP's in each stimulus category, ERP's were averaged to all the novels (N) together, targets (T) together, and only the non-targets immediately preceding the target stimuli. These stimuli were named Preceding Non-Targets (PNT), and are labelled as such in all figures.

RESULTS

A two-way analysis of variance with repeated measures on one factor was performed (Winer 1962). The amplitude of N1-P2 was significantly reduced in the alcoholics for all stimuli ($p < 0.02$), while the geriatric group fell midway between the controls and alcoholics (Figure 3). The geriatric group did not differ significantly from either the controls or alcoholics for N1-P2 amplitude.



RUN 2

Figure 3. Mean N1-P2 amplitude for the target (T), non-target (PNT) and novel (N) stimuli for the three groups of subjects: controls (—), alcoholics (- - -), and geriatrics (.....).

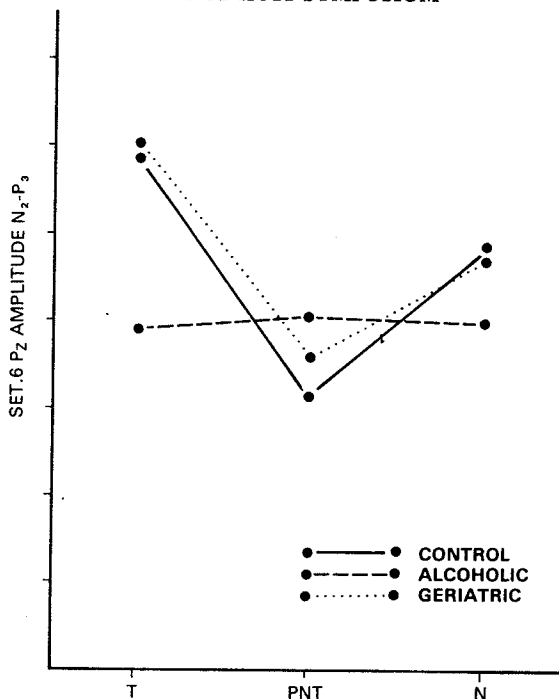


Figure 4. Mean amplitude of N2-P3 for the three stimulus categories (target, non-target and novel) in the three subject groups: control (—), alcoholic (---), geriatric (....).

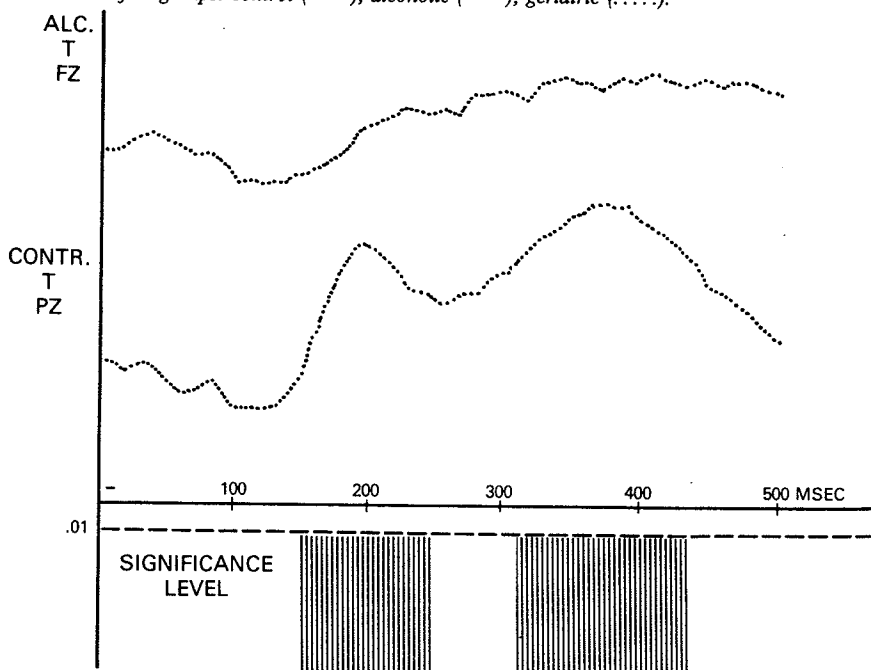


Figure 5. Grand mean ERP's to target stimuli for the alcoholics (top trace) and controls (bottom trace). Significant differences ($p < 0.01$) between the two curves as performed with point-by-point t-tests is indicated below the ERP traces.

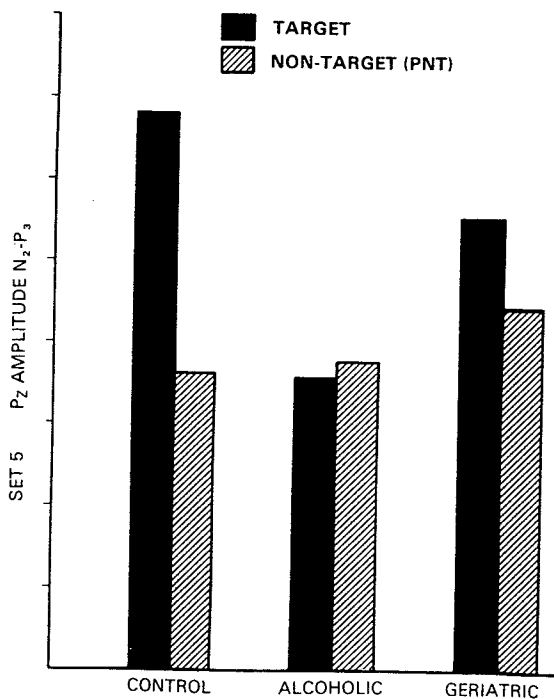


Figure 6. Mean ERP amplitude N2-P3 to target (■) and non-target (▨) stimuli for the three groups of subjects: control, alcoholic and geriatric.

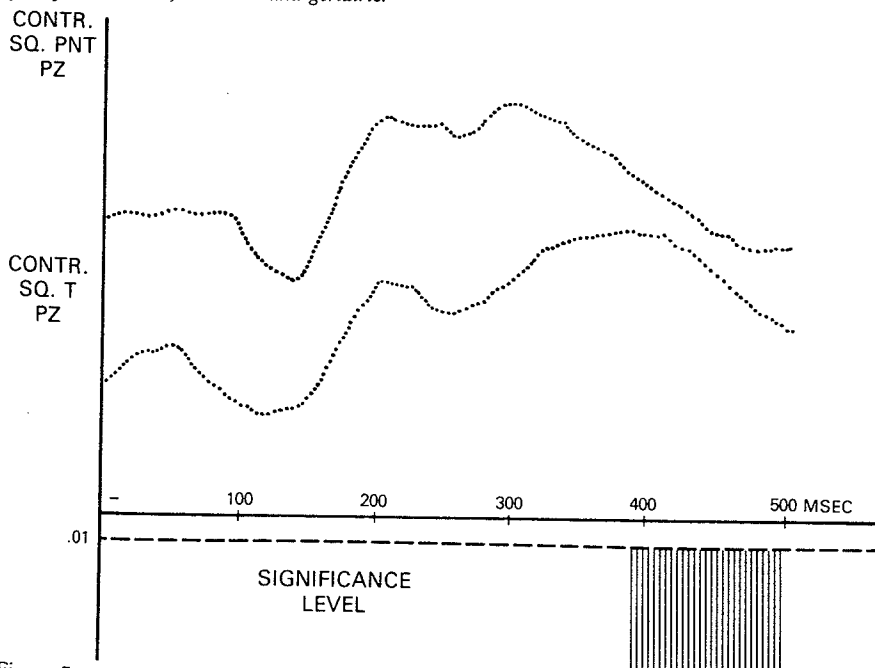


Figure 7. Grand mean ERP waveforms recorded to the same stimulus (square) when it served as a target (bottom trace) or non-target (top trace).

As indicated in Figure 4, the amplitude of N2-P3 was also found to be significantly smaller in the alcoholic subjects to the target stimuli only, both in comparison with the control group (at $p < 0.001$) and the geriatric group (at $p < 0.02$). No significant amplitude difference existed between groups for PNT and N stimuli. Amplitude N2-P3 was not statistically different between old people and normal controls.

A comparison of parietal gland mean ERP waveforms to target stimuli in alcoholic and control is illustrated in Figure 5. Point-by-point t-tests between these waveforms indicated that the points occurring between 155 and 245 msec, and the points between 315 and 435 msec were highly significant between these two groups ($p < 0.01$). These points correspond to N1-P2 and N2-P3, respectively.

The amplitude of N2-P3 differed significantly across the three classes of stimuli in both the control group and the geriatric group (Figure 4); it was largest for the target, next largest for the novels, and smallest for the PNT ($P < 0.001$, controls; $p < 0.02$ geriatrics). As indicated in Figure 4, this was not

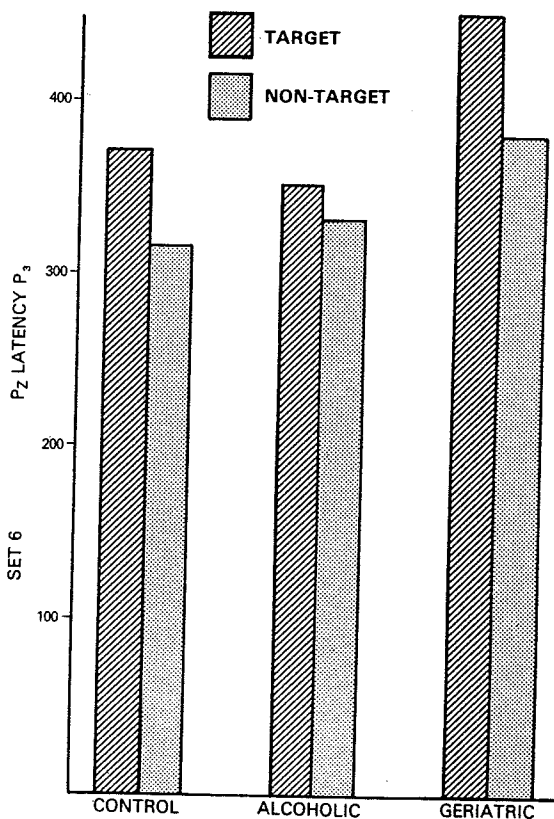


Figure 8. Mean P3 latency to the target and non-target stimuli for each group of subjects: control, alcoholic, geriatric.

the case for the alcoholic group who maintained the same low level P3 amplitude regardless of task.

The difference in P3 amplitude to target and non-target stimuli (PNT) is illustrated in Figure 6 for each of the groups of subjects. The P3 amplitude is significantly larger when the same stimulus serves as target than when it serves as a non-target in the control group ($p < 0.001$) and in the geriatric group ($p < 0.005$). There was no significant difference in P3 amplitude between T and NT in the alcoholic group.

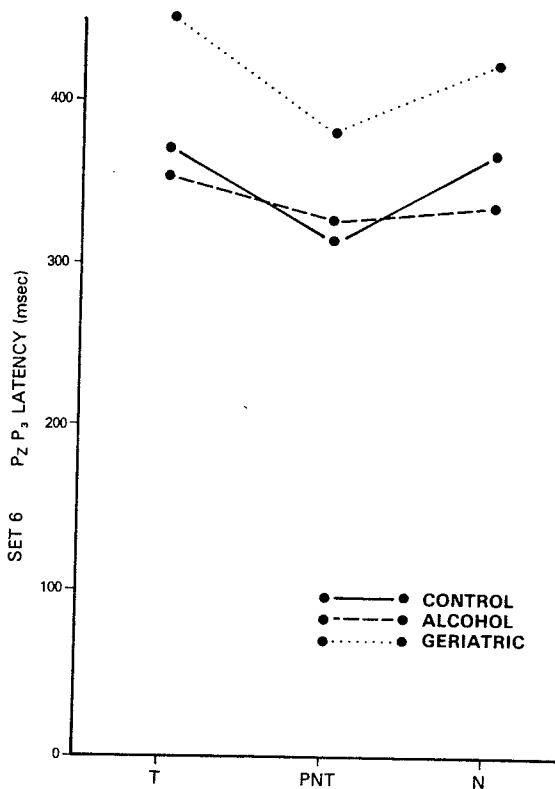


Figure 9. Mean latency of P3 to the target (T), non-target (PNT) and novel (N) stimuli in the control, alcoholic and geriatric groups of subjects.

The difference in waveform (P3 amplitude) to target or non-target stimuli in the control group is illustrated in Figure 7. As Figure 7 indicates, the P3 component is significantly larger when the square serves as a target (while N1-P2 amplitude is the same for the two stimulus categories). In addition, there is a latency shift in P3, which occurs significantly earlier when the stimulus is a non-target than when it is a target.

This phenomenon of latency shift in P3 latency to target and non-target

stimuli is illustrated in Fig. 8. There was a significant difference between P3 latency for target and non-target stimulus categories in both the control and geriatric groups ($p < 0.001$, control; $p < 0.001$, geriatric), while the difference in P3 latency between targets and non-targets in the alcoholic group was negligible.

As is indicated in Figure 9, P3 occurred significantly later in the geriatric group in comparison to each of the other two groups ($p < 0.001$) for all stimulus categories. On the other hand, the latency of P3 fell within the normal range for the chronic alcoholics.

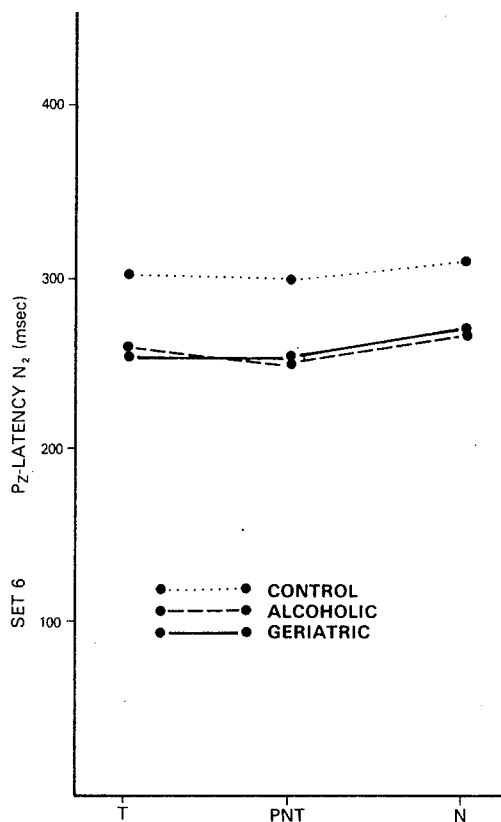


Figure 10. Mean latency of N2 for the three stimulus categories (target, non-target and novel) for the three subject groups (control, alcoholic and geriatric).

The latency of N2 also occurred significantly later in the geriatric group than the other two groups ($p < 0.001$ for T and N; $p < 0.02$ PNT). As Figure 10 indicates, latencies of N2 were virtually identical between the alcoholic and control group.

These latency shifts in the geriatric subjects are illustrated in a comparison of Figures 2 and 11 (group centroids). In the centroid for the control group

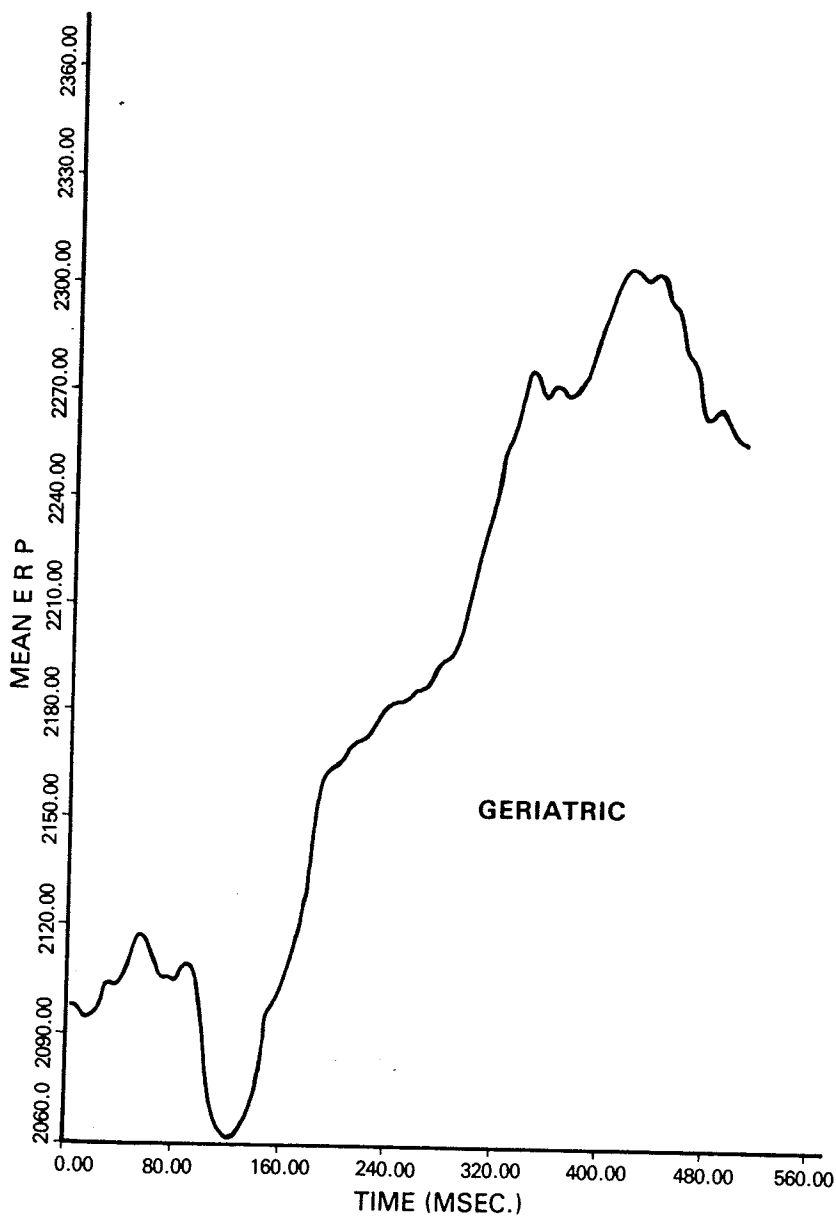


Figure 11. Centroid ERP of the geriatric group obtained by collapsing ERP's over midline electrodes (Fz, Cz, Pz, Oz) and over stimulus categories (T, PNT, N).

(Figure 2), all the components are clearly differentiated as follows: P1 (45 msec), N1 (115 msec), P2 (200 msec), N2 (235 msec) and P3 (335 msec). The P3 component occurs at 335 msec. Figure 11 illustrates the centroid of the geriatric group, indicating that the components occur significantly later than

the controls. There are major shifts in all latencies, but particularly the P3 component which occurs at 420 msec. This is 85 msec later than the control centroid.

DISCUSSION

The results of this study indicate that the late components (N1-P2 and N2-P3), are significantly decreased in amplitude in the chronic alcoholics. These late components are of normal amplitude in the elderly subjects, but occur significantly later. Thus it appears that while ERP's in both groups differ from those of young healthy controls, the nature of their aberration is different.

In the ERP literature, the N1-P2 component differentiates between the attended and unattended channel (for example visual and auditory modalities) (Hillyard 1978). It is enhanced to all stimuli in the attended channel, regardless of whether they are targets or not. In this particular study, all the stimuli were in the relevant channel, namely the visual stimulus modality, and therefore all amplitudes are expected to be enhanced. However, as can be seen in Figure 3, the amplitudes of the alcoholics are depressed to levels comparable to responses in an irrelevant stimulus modality. This is consistent with our previous bimodal N1-P2 experiment (Porjesz & Begleiter 1979), where we found that alcoholics did not manifest differentially enhanced N1-P2 components to stimuli in the relevant as opposed to the irrelevant stimulus modality, but maintained the same low amplitude response regardless of stimulus relevance. Taken together, these studies both suggest that "sensory filtering" mechanisms are impaired in chronic alcoholics.

While the N1-P2 amplitude for the elderly subjects did not differ significantly from the control group, it occurred significantly later than in the other groups. This suggests that while their "sensory filtering" mechanisms are intact, old people need more time to differentiate relevant from irrelevant material.

Results from the ERP literature indicate that the P3 component is expected to be enhanced if the stimulus is in the relevant channel *and* is the target *signal* (Donchin 1979). The finding that P3 amplitudes are similar in old people and normal controls indicates that old people are able to probability-match as well as young people. The P3 amplitude was significantly larger and later to target than non-target stimuli in both the control group and elderly group. This indicates that old people are able to respond to relevant target stimuli and attenuate responding to irrelevant stimuli. On the other hand, in contrast to the other two groups, the alcoholics maintained the same low amplitude and identical latencies of P3 to both target and non-target stimuli, regardless of stimulus relevance. Thus they seem to be unable to differentially respond to relevant and irrelevant inputs. Again, this seems to indicate a deficit in "sensory filtering" in chronic alcoholics, and an inability to utilize available information.

As P3 latency reflects amount of time necessary to make a decision, the significantly longer P3 latency in the elderly group suggests that old people are slower in deciding whether a stimulus is target. P3 latencies have been found to

correlate with reaction time latencies (*Kutas et al. 1977, Squires et al. 1977, Ritter et al. 1972*) and both of these seem to increase with age (*Benton 1977*).

Our findings that P3 occurs later in old people without concomitant amplitude decrements has been recently independently reported in several different laboratories (*Brent et al. 1976, Smith et al. 1976, Ford et al. 1979*). In one normative P3 study (*Goodin et al. 1978*) of ERP changes related to age, the rate of delay in latency with age was found to be 0.7 msec/year for P2, 0.8 msec/year for N2 and as high as 1.8 msec/year for P3.

It seems, therefore, that both the alcoholic and elderly groups manifest electrophysiological brain dysfunction that appears to involve higher integrative centers of the brain. In terms of behavioral performance, both groups were more similar to each other than to the control group, having most difficulty responding to target stimuli. However, although both groups resembled each other behaviorally, they were quite different from each other electrophysiologically. The major ERP aberrations in the alcoholic group (in contrast to both other groups) were: (1) the lack of differentiation between their responses to relevant and irrelevant inputs, and (2) the low voltages of their event-related brain activity. While the major electrophysiological aberration in the alcoholic subjects is one of voltage, the major electrophysiological dysfunction in the geriatric subjects is one of latency. The alcoholics manifest impaired sensory filtering and probability-matching processes (responding identically to infrequent relevant and frequent irrelevant inputs), while the geriatric subjects differentiate between relevant and irrelevant inputs. The geriatric subjects, on the other hand, exhibit impaired stimulus evaluative mechanisms with regard to *speed* of evaluation, requiring a longer period of time to determine the relevance of a stimulus.

Thus, on the basis of this information-processing event-related-potential experiment, it was concluded that while ERP's in both alcoholic and geriatric subjects differ from those of young, healthy controls, the nature of brain dysfunction is different. Despite behavioral similarities between alcohol-related deficits and those of the aging process, the underlying neurophysiological aberrations are quite different in the two groups, and suggest caution in postulating a common neuropathological mechanism.

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