

## EVENT-RELATED POTENTIAL CHANGES IN HEALTHY AGED FEMALES<sup>1</sup>

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Changes in cognitive function among the elderly are often the result of specific diseases affecting brain function. The central nervous system (CNS) may also undergo changes with aging that are independent of specific disease but are the result of the aging process itself. Separating these two factors is a difficult task, especially in living humans, but any success in this endeavor would provide insight into the biological process of aging.

Electroencephalographic event-related potentials (ERPs) provide a non-invasive method of observing neurophysiological events in the CNS. The early components (up to 125 msec) of the ERPs to visual, somatosensory, and auditory stimuli are increased in amplitude in the elderly (Dustman and Beck 1966, 1969; Lüders 1970; Brent et al. 1977). These changes are sometimes greater in patients with decreased mental functioning (Straumanis et al. 1965). Most of these studies demonstrating differences in ERP amplitude and latency between old and young subjects have used stimuli of a single intensity. Collection of responses to stimuli over a range of intensities provides additional information (Picton et al. 1977) that might demonstrate more fully neurophysiological changes accompanying the aging process.

This report presents the results of an inves-

tigation designed to delineate CNS changes reflected by ERPs in healthy elderly subjects who have a high level of cognitive functioning and who have no evidence of specific diseases affecting the CNS. When these subjects were compared to young controls, we found that some neurophysiological response measures were increased, some were diminished, and others were the same.

### Methods

A group of 9 elderly healthy females between the ages of 74 and 87 years (mean 78.9) were matched for educational level with 9 young healthy females between the ages of 20 and 28 (mean 22.7). All subjects were given a physical examination and none were included who had active symptoms of cardiovascular, respiratory, renal, gastrointestinal, or endocrine disease. The elderly subjects were remarkable in that they had histories of little or no significant disease and were extremely healthy for their age. All the subjects also had relatively intact auditory acuity with auditory sensation thresholds less than 30 dB sound pressure level (SPL) at 500 Hz. All subjects were given the Wechsler Adult Intelligence Scale (WAIS). The unadjusted scores converted to mean IQ equivalents of 121 for the young and 104 for the elderly subjects using the 20–24-year-old norms. When the 75-year-old norms were applied to the elderly

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subjects, their mean IQ was 128 (Wechsler 1955). Average years of school were 16.6 for the elderly and 15.8 for the young subjects.

The electro-oculogram (EOG) and frontal (Fz), central (Cz), and parietal (Pz) electroencephalogram (EEG) were recorded while auditory stimuli were delivered. The nominal bandpass for the amplifiers was 0.03–100 Hz (3 dB points of 6 dB/octave rolloff curves). The stimuli were 500 msec duration, 500 Hz tones of 4 different intensities presented in a random order every 1500 msec. The sensation threshold was determined for each subject and the stimuli were adjusted individually to be 60, 70, 80 and 90 dB above threshold. ERPs were created by averaging the EEG response to 64 presentations of each stimulus intensity. During the stimulus presentation, the subjects read a large-print book. Afterward, they were given a quiz about the passage they had read.

Three major peaks (P1, N1, P2) and the late sustained potential (SP) were identified for each subject for each ERP. The amplitude (defined as the peak deviation from the pre-stimulus baseline) and the latency of the maximum positive peak between 16 and 72 msec (P1), maximum negative peak between P1 and 136 msec (N1), and the maximum positive peak between N1 and 216 msec (P2) were identified by a computer algorithm. The SP was derived by computing the mean deviation from baseline for the 300–450 msec epoch of the ERP. The effects of age, intensity and recording site on the amplitude and latency of each component were estimated by analysis of variance (BMD-08V).

## Results

Fig. 1 presents grand averages for the young and elderly subjects superimposed. Figs. 2 and 3 present the amplitude and latency values for the P1, N1 and P2 components. Fig. 4 presents the SP values for the two groups.

The greatest differences between the old

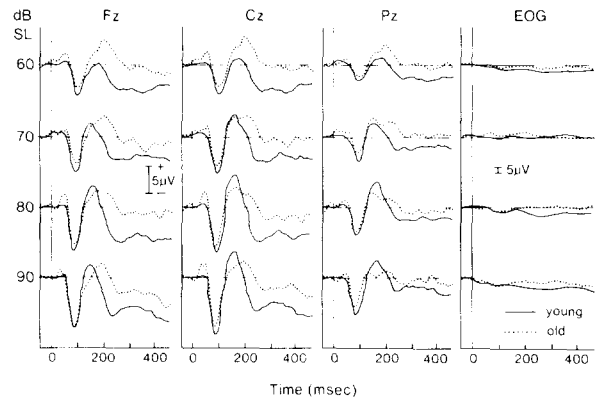


Fig. 1. Group AEPs for 9 old and 9 young subjects to stimuli of 60, 70, 80 and 90 dB SL recorded from Fz, Cz, Pz and associated EOGs. Each wave consists of a total of 576 individual trials.

and young subjects were found in the later components of the ERPs. The SP was most prominent at Fz and Cz (lead effect:  $P < 0.001$ ), and it was significantly smaller in the

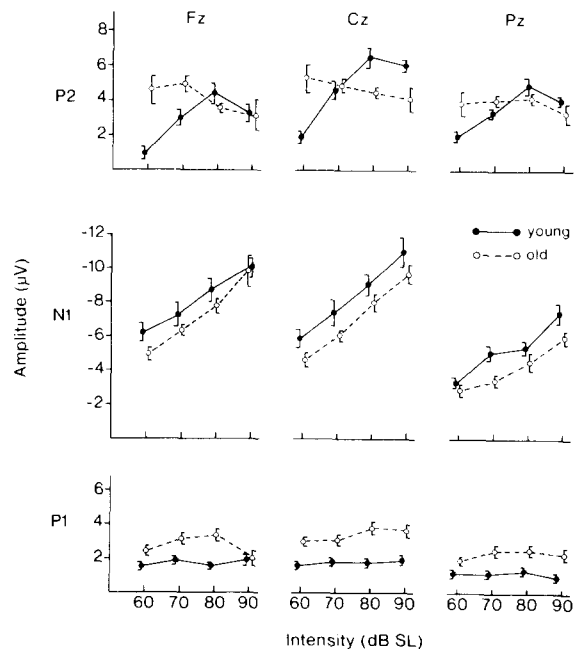


Fig. 2. Means and standard errors for amplitude of P1, N1 and P2 components of AEPs to stimuli of 60, 70, 80 and 90 dB SL recorded from Fz, Cz and Pz electrode placements for old and young subjects.

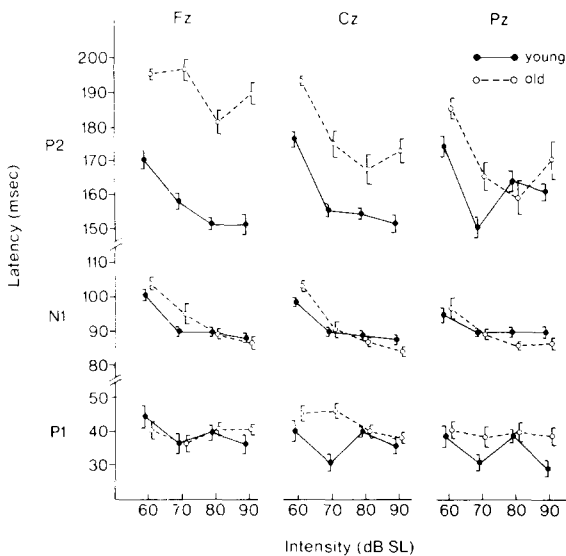


Fig. 3. Means and standard errors for latency of P1, N1 and P2 components of AEPs to stimuli of 60, 70, 80 and 90 dB SL recorded from Fz, Cz and Pz electrode placements in old and young subjects.

aged subjects ( $P < 0.001$ ). The P2 component was later in latency for the aged subjects ( $P < 0.001$ ), and this effect was most prominent at the Fz (age  $\times$  lead interaction:  $P < 0.01$ ). For the young subjects, the amplitude of P2 increased with increasing stimulus intensity up to 80 dB and then it saturated (or even decreased in amplitude) for the 90 dB stimulus (intensity effect:  $P < 0.001$ ). This

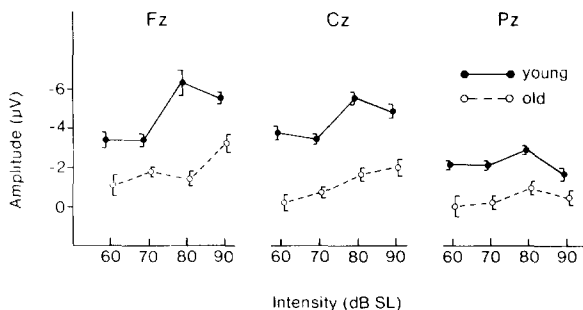


Fig. 4. Means and standard errors for amplitude of SP component of AEPs to stimuli of 60, 70, 80 and 90 dB SL recorded from Pz, Cz, and Pz electrode placements in old and young subjects.

same orderly effect of stimulus intensity on P2 amplitude did not occur for the aged subjects (age  $\times$  intensity interaction:  $P < 0.05$ ). Unlike the P2 component, N1 increased in amplitude ( $P < 0.001$ ) and decreased in latency ( $P < 0.001$ ) across the entire range of stimulus intensities for both groups. There was no difference in N1 amplitude or latency between the old and young subjects. The earliest component measured (P1) was unaffected by stimulus intensity, but it also revealed age-related changes in amplitude; the aged subjects had a larger P1 amplitude than the young ( $P < 0.05$ ).

## Discussion

Although the specific neuroanatomical explanation for the changes found in this study must await more research into ERP generator sources, the results are offered as more evidence that there are age-related changes in the CNS that can be demonstrated electrophysiologically. The fact that one component was unaltered in the aged group (N1), while others were enhanced (P1), diminished (SP), or revealed a disturbance in the orderly response to a range of stimuli (P2), suggests that the changes are not merely non-specific degradation of physiological processes.

Differences in attention paid to the task between the two groups might account for some of the ERP differences. The scores on the post-session quiz showed that the old subjects read more slowly than the young (4.3 pages versus 6.1 pages) and answered fewer questions correctly (67% versus 96%). Thus, both groups did better than chance (25%) on the multiple-choice quiz. This suggests that both groups did attend to the reading task, but the young subjects performed better at it. It has been shown that N1 amplitude can be an index of attention (Hillyard et al. 1973; Picton and Hillyard 1974). The lack of significant difference in N1 amplitude (both when measured from baseline to N1 and from P1 to N1) between old and young subjects in this

study suggests that attention was similar in both groups. Another study with these same subjects, in which an auditory selective attention task was performed, also revealed no significant difference in N1 amplitude between young and old (Ford et al. 1978).

The 'middle latency components' (8–50 msec) have been shown to be quite susceptible to myogenic contamination (Picton et al. 1974). The early positive component, which we labeled P1, had a mean latency of 40 msec which puts it in this class. It is possible that the P1 component presented here is actually a combination of the Pa component with a usual latency of about 30 msec, and the P1, which usually has a latency of about 50 msec and forms part of the P1-N1-P2 vertex potential complex. This might be of particular concern in the interpretation of these data because the old subjects who had larger P1s also had higher auditory thresholds (young = 4.2 dB at 500 Hz; old = 18.0 dB at 500 Hz). This group, therefore, received physically stronger stimuli, although the perceived auditory intensities were the same as for the young subjects. This might have contributed to a larger myogenic component which can be mediated through vestibular rather than cochlear receptors (Townsend and Cody 1971). Arguing against a myogenic response as the explanation for the increased P1 in the older subjects is the fact that myogenic contaminants are more pronounced at high intensities. The data from this study, however, demonstrate significantly larger P1 for the old subjects across all intensities, and there is virtually no increase in amplitude with increasing stimulus intensity.

Localization of the generators of these ERP components would help considerably in interpreting their significance. Unfortunately, there is only speculation about their origins. It has been proposed that components with the latency of the P1 component identified in this study (40 msec) may be generated by the thalamus and/or primary sensory cortex (Picton et al. 1974). The N1 and P2 components of the auditory ERP are thought to be

primarily cortical in origin and result from activity in the frontal association cortex. The SP is maximal at frontal recording sites and is similar in wave form to other 'slow potentials' such as components of the contingent negative variation (CNV) and the 'readiness' or Bereitschaft Potential (BP) (Järvilehto and Frühstorfer 1973; Picton et al. 1977). Deeke et al. (1976) have suggested that the CNV and BP have their origins in the dendritic network of the upper cortical layers and that increasing negativity at the scalp indicates an increase in CNS activity in these layers.

The sustained potential is most evident after about 250 msec when the P1-N1-P2 complex is over. It may begin much sooner, however, and be obscured by the earlier components. If it began as early as P1, the significantly smaller P1 and the larger (but not significant) N1 seen in the young group as compared to the old could be due to the influence of the SP. Since the sustained potential is greater for the young subjects, it could 'pull down' P1 and increase N1 negativity in those subjects. It also appears to have similar effects on P2, especially at the low intensities (see Fig. 1, Fz, 60 dB). Additional analyses were performed on the P1 to N1 amplitude and the N1 to P2 amplitude in order to investigate this hypothesis. While the absolute amplitude from the baseline to P1 was significantly larger for the old subjects, the P1 to N1 amplitude was not. The N1 to P2 amplitude measure, however, again produced a group  $\times$  intensity effect ( $P < 0.02$ ), as was the case with the baseline to P2 measure. Thus the influence of the SP might explain the P1 amplitude difference but cannot account for the P2 stimulus intensity-response amplitude difference between the two groups.

It is difficult to posit a single deficit to explain the age-related differences found in this study. The larger P1 in the aged could result from a loss of cortical inhibitory influences on the putative subcortical generators of the early ERP components. However, it can as easily be attributed to the algebraic results of the diminished SP, and an unaltered

P1. This diminished SP might result from a postulated loss in dendritic mass, especially in frontal and temporal cortex. Scheibel and Scheibel (Scheibel and Scheibel 1975; Scheibel et al. 1975) have presented histologic evidence for the progressive loss of the horizontal dendritic system as a function of both age and senility and observed that considerable loss can occur without noticeable clinical results. If the frontally distributed slow waves, such as the SP and CNV, do have their origins in dendritic networks, our electrophysiologic observations would be consistent with the histologic data. The lack of the orderly stimulus intensity-response amplitude function in the aged group is more difficult to account for, however. The SP does have an algebraic influence on P2, but cannot completely explain the group difference seen in P2.

The fact that these age-related differences were found in a group of extraordinarily healthy and active subjects lends support to the claim that these differences are due to age rather than to specific pathological states. However, occult pathology must always be considered as a possible contributor to the findings. The neurophysiological differences between young and old subjects are compatible with the histologic differences presented by Scheibel et al. (1975) in both senile and non-senile brains. ERPs offer a non-invasive method for assessing age-related neurophysiological changes before the appearance of concomitant clinical manifestations.

### Summary

Neurophysiological changes in the central nervous system were demonstrated with EEG event-related potentials in healthy, aged women. Compared to young women, the aged women showed decreased amplitude of the late sustained potential (SP), increased P2 latency, disruption of the normal stimulus intensity-response amplitude function of P2, and increased amplitude of the P1 compo-

nent. These age-related changes are interpreted as neurophysiological reflections of CNS deterioration found in non-senile elderly persons.

### Résumé

#### *Modifications des potentiels liés aux événements chez des femmes âgées bien portantes*

Des modifications neurophysiologiques du système nerveux central ont été mises en évidence à l'aide des potentiels EEG liés aux événements chez des femmes âgées bien portantes. Par comparaison à des femmes jeunes, on observe chez les femmes âgées une amplitude diminuée du potentiel tardif prolongé (SP), une latence accrue de P2, une discontinuité de la fonction normale intensité de stimulation-amplitude de la réponse P2, et une amplitude accrue de la composante P1. Ces modifications sont interprétées comme le reflet neurophysiologique de la détérioration du système nerveux central qui s'observe chez des personnes âgées non-séniles.

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