

# P300 and Neuropsychological Tests as Measures of Aging: Scalp Topography and Cognitive Changes

Anders M. Fjell\* and Kristine B. Walhovd\*

**Summary:** The rationale for the present study was to investigate several aspects of P300 topography in relation to aging and neuropsychological measures. We administered an auditory oddball ERP task to 72 participants aged 21.8 to 94.7 years, 36 males and 36 females, in addition to the Wechsler Abbreviated Scales of Intelligence (WASI) and digit span from the Wechsler Adult Intelligence Scales – Revised (WAIS-R). The relationship between age and P300 latency and amplitude at different electrodes was investigated, as well as the changes in the correlational pattern between P300 latency and amplitude with increasing age. A formal test of curvilinear relationships for P300 latency / amplitude and age was performed. Principal component factor analyses were performed for P300 latency and amplitude separately in order to check for possible superordinate structures in the distribution of the electrical activity measured at the scalp. In addition, each of the electrodes and each of the factors were correlated with the different neuropsychological measures, and the contribution of age to the observed relationships is discussed. The main conclusion drawn is that the activity generated from different brain areas change at different rates with age. While the posterior area shows a clear reduction of P300 amplitude and a delay of P300 latency with age, the amplitude does not decrease at the same rate in the fronto-central areas, and there is at the same time a marked hemispheric asymmetry in the age dependent change of activation. Based on our data, it may be concluded that a curvilinear expression generally does not explain the aging effect on the ERP component P300. Correlations between neuropsychological measures and P300 did, as expected, vary with area of activation, and the strongest correlations were generally found between matrices, block design and digit span, and the midline and left fronto-temporal electrodes. These relationships were in turn mediated by age. Implications of the findings are discussed.

**Key words:** P300; Aging; Neuropsychological measures; Cognitive measures; ERP.

## Introduction

In studies of cognitive aging, efforts have been made to produce normative as well as patient group data for a broad age spectrum on the endogenous electrophysiological components typically elicited to certain types of stimuli, so called event-related potentials (ERPs) (e.g., Barrett et al. 1987; Brown et al. 1983; Fein and Turetsky 1989; Goodin et al. 1978a; Goodin et al. 1978b; Hömberg et al. 1986; Iragui et al. 1993; Patterson et al. 1988; Picton et al. 1984; Polich et al. 1986; Polich et al. 1990; Verleger et al. 1992). The ERP component P300 is consid-

ered a cognitive neuroelectrical indicator of CNS activity (Regan 1989), involved with the processing of new information when attention is engaged to update memory representations (Polich 1996). P300 latency can be regarded as a measure of the relative timing of the stimulus evaluation process, indicating an upper limit on categorization and stimulus evaluation time (Coles et al. 1995), or the time taken to allocate resources and engage memory updating. P300 amplitude is held to index attentional resource allocation when memory updating is engaged (Polich 1996). ERPs constitute the only noninvasive method that resolves the dynamic pattern of events in the human brain down to the millisecond range, and may define a valuable framework within which behavioral or introspective data may be interpreted (Brandeis and Lehman 1986).

The question of scalp distribution effects of P300 amplitude and latency is of considerable importance in addressing the question of which specific neural generators may underlie the P300 component. It is reasonable to assume that surface EEG predominantly reflects the activity of cortical neurons close to the particular electrode (Westbrook 2000). This does, however, depend both on differences in the depth and orientation of the neurons, as well as individual variability in craniocerebral topography (Steinmetz et al. 1989). The exact relationship between

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ERPs measured at the scalp and the corresponding processes in the brain is not yet fully understood (Paller et al. 1992). Depth electrode and magnetic field studies (Halgren et al. 1980; Okada et al. 1983; Shinba 1999), as well as studies of source localization (Tarkka and Stokic 1998), suggest that the P300 component reflects electrical events originating in the medial temporal areas, most likely including the hippocampal structures and the amygdala. The component should thus be related to tasks with high memory demands. However, patient group studies involving damage due to temporal lobectomy or stroke, as well as animal studies, have indicated that the hippocampal formation and the surrounding areas in the medial temporal lobe influence the scalp recordings of P300 only to a relatively modest extent (Paller et al. 1992; Polich and Squire 1993). The hippocampal formation is located inside the medial temporal lobe, and so it may be difficult to measure hippocampal activity at the scalp. Paller et al. (1992) argue that neural generators not dependent upon the medial temporal lobe are responsible for most of the P300 obtained in scalp recordings, but the same events that activate these generators also instigate medial temporal lobe activity. The recommendation that P300 should be measured at Pz (Picton et al. 2000), reflects the fact that this component, at least in young subjects, is best observed parietally (Friedman et al. 1997; Polich and Heine 1996).

Polich and Kok (1995) suggest that multiple neural sources contribute to the observed scalp topography of the P300. Ji et al. (1999) support the hypothesis of multiple generators of P300, and argue that these generators are not symmetrically distributed across the two hemispheres. Alexander et al. (1995) also report P300 amplitude hemispheric asymmetry. One question is then what happens to the distribution of activity with aging. Bellis et al. (2000) observed that in elderly subjects, evoked responses to speech sounds (the P1-N1 complex) had a symmetrical distribution of amplitude across the hemispheres, in contrast to the distribution found in a group of children, as well as in a group of young adults. Bellis et al. interpret this as representing a biological, age-related change in the neural processing.

Aging studies of ERP scalp topography generally show a gradual shift in activation from posterior to anterior areas, that is, a more even distribution of activity with age (Anderer et al. 1996; Friedman et al. 1997; Iragui et al. 1993; Pfefferbaum et al. 1984; Vesco et al. 1993). An important question regards the functional correlates to this shift. Vesco et al. (1993) indicate that the more even scalp distribution of P300 amplitude in high age may be a result of differential effects of age on frontal and parietal generators of the P300. They argue in favor of a multiple generator view of P300, implying a frontal generator that is more prone to aging. Alternatively, as suggested by Fabiani and Friedman (1995), it is possible that a common

integrated neural generator circuit, i.e. an anterior-posterior neural network, may be differentially activated depending on the stimuli. The frontal generators of this hypothesized neural circuit may be activated the first few times a stimulus is presented, though not activated to the same degree when the stimulus is presented a greater number of times. Differential rates of adaptation to new stimuli can thus explain the differential patterns of activation observed for young and elderly subjects. Friedman et al. (1997) argue that the frontal activity in elderly persons is consistent with both the hypothesis that older adults cannot inhibit a «novelty» response, as well as the hypothesis that it takes older adults longer to form and maintain an adequate representation of rarely occurring stimuli in working memory. Balota et al. (2000) have indicated that frontal areas can be tied to both attention, working memory, and inhibition control, three aspects of cognitive aging.

It is not likely that the topographical alterations in P300 across age are related to gross alterations of brain structures (Friedman et al. 1997). Studies employing regression analyses indicate that volumetric measurements of brain structures account for only a small proportion of the variance in P300 scalp topography. The reported changes in topography must then mainly be due to differences in functional processing. Psychometric tests have also been applied in a wide range of studies in order to investigate cognitive changes with age (Babcock and Laguna 1996; Birren and Schroots 1996; Brébion et al. 1997; Grégoire and Van der Linden 1997; Kausler 1991; Papalia et al. 1996; Park 2000; Woodruff-Pak 1997), but the relationship between cognitive tests and ERP measures in relation to aging still needs to be examined.

As a method for studying neurophysiological generators of P300, Polich et al. (1997) have argued that the topography of P300 amplitude and latency correlations could index component scalp distribution differences that reflect the size and/or orientation of the underlying generator(s). In a young sample, auditory P300 amplitude and latency were the most negatively correlated and tightly coupled over the frontal-central and medial-lateral recording sites.

The aim of the study

#### *Effects of age on P300- topography*

There is a lack of ERP studies of aging that systematically investigate the effects of age on other recording sites than the central line (Fz, Cz, Pz). We wanted to include more electrodes, to be able to investigate the contribution of age to topographic variations in P300 amplitude and latency. Of the electrodes on the central line, Fz is found to correlate the least with age. A question that still needs to be answered, however, is whether this posterior-anterior

shift with age is found for both hemispheres, that is, at the recording sites lateral to the midline electrodes. As discussed above, there are reasons to expect lateralization differences in processing, and these should lend themselves to ERP-investigation in aging studies.

In the ERP paradigm employed in our study the subject is asked to count target tones, and this task involves focused attention and memory updating and maintenance (see below). These processes possess qualities similar to verbal short-term memory tasks, known to depend heavily on frontal and left hemisphere structures (D'Esposito et al. 1999; Iidaka et al. 2000; Springer and Deutsch 1998). Low et al. (1999), in a visual ERP-study, employing source modeling, found activity in anterior areas under high working memory load, and posterior activity under low working memory load, in addition to a general shift in activity from right to left under high, compared to low working memory load. However, in another visual ERP study, Ranganath and Paller (2000) found that both left and right prefrontal regions were engaged when demands to retrieve and evaluate perceptual information were increased. Still, the left prefrontal involvement is likely to be stronger in verbal and auditory than in visual tasks. We would thus expect a weaker relationship between age and frontal ERP parameters for the left hemisphere as opposed to the right, given that the task depends more on left hemisphere structures and that the working memory demands will make the task more difficult for the older part of the sample. Regarding the more posterior recording sites, we would expect a strong association between age and the central and parietal lateral electrodes. The temporal recording sites are known to generally yield weaker P300-measures, and so we do not expect these to demonstrate any strong relationship with age.

#### *Superordinate structures*

We also wanted to check for superordinate structures. Factor analysis may play a part in ERP-studies employing more than just a few electrodes. In these cases, doing analysis on the levels of factors may turn out more reliable than a focus on single electrodes. In addition, it is important to investigate which electrodes tend to cluster, whether the clusters of electrodes are the same with regard to latency as to amplitude, whether lateralization differences are evident, and whether the clusters of electrodes show correlations with age and neuropsychological measures of the same magnitude as the single electrodes. As described above, ERP studies have indicated hemispheric differences in homogenous samples, and studies in experimental cognitive psychology (e.g. Chokron et al. 2000) have shown hemispheric specialization for selective attention. We expect that the patterns of activation will differ for each side of the

midline, and that these differences will be mediated by age. These inter-hemispheric differences are likely to yield separate factors for each hemisphere. The remaining variance then should be explained by factors covering the midline area. Our predictions concerning which electrodes will tend to show similar patterns of activation thus include at least one lateral factor covering each hemisphere, as well as one or more factors covering the midline brain areas.

#### *Neural generators*

A related question concerns the findings by Polich et al. (1997), that P300 amplitude and latency were most negatively correlated and tightly coupled over the frontal-central and medial-lateral recording sites in a sample with minimal variation in age. The authors argue that the size of the correlations function as indicators of the neuronal generation potency. As cited above, however, earlier studies point to a tendency for P300 amplitude to increase anteriorly relatively to parietally with age, while such a differential anterior vs. parietal pattern is not to the same degree seen for latency. We thus expect the pattern of correlations over the midline electrodes to change with age. An important question is whether the overall pattern of topography, that is, for other electrodes than the midline ones, will change with age. If so, this would imply either that there is reason to doubt Polich et al.'s (1997) view of this method's suitability in identifying neuronal generator potency, or that the pattern of neuronal generator potency changes with age.

#### *P300-topography, neuropsychological measures, and aging*

Relations between ERP measures and cognitive/neuropsychological measures have been reported (e.g. Egan et al. 1994; O'Donnell et al. 1992; Pelosi et al. 1992; Reinvang 1999; Walhovd and Fjell 2001). An interesting question regards to which extent the relationship between activation recorded from various scalp areas and neuropsychological measures is affected by variations in age. For instance, digit span is found to correlate with age (Brébion et al. 1997; Grégoire and Van der Linden 1997) and with ERP measures (Polich et al. 1983). What is not known is whether variations in age explain the same variance in digit span as in ERP measures. This question is not easily answered by the standard procedure of regression analysis. When, for instance, both P300 amplitude and digit span correlate with each other, and at the same time steadily decrease with age, an analysis of regression will indicate that age may explain the observed relationship between digit span and P300 amplitude. However, it is still possible that a relationship between P300 amplitude and digit span exists independently of age. Since both measures correlate with age,

however, this relationship will not be evident in an analysis of regression. Still, it is an important question how the relationship between neuropsychological measures and ERP measures may be understood in light of the aging process. This question may be addressed by comparing the topographic pattern of test performance/P300 correlations with the pattern of age/P300 correlations. If the patterns correlations differ, this may indicate that different processes underlie the age dependent changes in P300 amplitude/latency and the test.

### *Curvilinearity in aging*

It is not known how the question of linearity/curvilinearity in electrophysiological aging should be answered. Some have reported that the relationship between electrophysiological measures and aging can best be understood as curvilinear (e.g., Beck et al. 1980; Brown et al. 1983), while most have found that it is better understood as linear (e.g., Michalewski et al. 1982; Picton et al. 1984; Polich 1996). Our even distribution of subjects across age, especially in the middle ages, allows us to perform a formal test of curvilinearity. In another publication based on this study (Walhovd and Fjell 2001), we demonstrated that while the slope of the aging curve of Pz is best explained by a linear equation, the decline in scores on various neuropsychological tests (block design, matrices, similarities) is best described by a curvilinear regression line. This means that the shape of the regression slopes differ for neuroelectrical and neuropsychological measures. One explanation for this discrepancy is that performance on the neuropsychological tests does not depend upon the same brain structures that generate the electric activity measured at Pz. It might be the case, then, that other electrodes show a curvilinear relationship with age. If this is so, one might speculate that these electrodes show neuroelectrical aging effects resembling the changing pattern of performance on certain neuropsychological tests with age to a greater extent than the midline electrodes do. This, in turn, may indicate that the electrical activity such electrodes are detecting, is more closely connected to performance on certain neuropsychological tests than the electric activity detected by Pz. The question of whether there are some electrodes that exhibit a curvilinear relationship with age and some that do not is crucial, but has not been properly investigated in the past.

## **Methods**

### **Sample**

The subjects were 72 healthy volunteers, 36 females and 36 males, recruited either on campus, through charity organizations, or activity centers for the elderly. All

subjects were given a moderate sum of money intended to refund possible costs related to their participation. Subjects' age ranged from 21.8 to 94.7 ( $m = 57.6$ ), and mean years of education was 14.3 ( $S.D. = 2.9$ ).

For the purpose of analysis, we chose to place the subjects in five categories, each covering 15 years; 19 subjects were between 20 and 34 years old (9 F/10 M, mean education = 14.7), 9 were between 35 and 49 (3 F/6 M, mean education = 16.5), 12 were between 50 and 64 (5 F/7 M, mean education = 15.5), 15 were between 65 and 79 (9 F/6 M, mean education = 14.0), and 17 were between 80 and 94 (10 F/7 M, mean education = 12.1). Polich (1996) recommends that aging studies use samples that are of equal density (ratio < 1.5). A satisfactory density ratio is necessary if one wants to investigate linearity/curvilinearity. We quantified the density of our sample by counting the number of subjects in each age-category. The ratio of the number of subjects in each group to every other group was then computed, and the mean of this ratio across all decades within the study was used as a measure of general subject density. With the use of 5 groups each covering 15 years, the density was 1.37.

Criteria for exclusion from the study were reported neurological diseases or injuries; Parkinson's disease, multiple sclerosis, dementia, major stroke, head trauma, or using a hearing aid. Subjects accepted for inclusion were then further given a short structured interview in which they were asked to report certain other factors which may affect cognitive aging or ERP measures: level of education, marital status, including whether they were widows/widowers/divorced and time of bereavement, whether they suffered from any chronic illnesses, regularly were on medication, smoking habits, exercise, CNS and medical history (e.g., having had mild concussion of the brain or general anesthesia during one's lifetime), and interval since last meal prior to recording (Geisler and Polich 1992; Papalia et al. 1996).

### **Cognitive tests**

In order to screen for dementia and also to obtain a valid measure of cognitive functioning, a Norwegian version of the Wechsler Abbreviated Scale of Intelligence, WASI (1999), and digit span from the Wechsler Adult Intelligence Scale – Revised, WAIS-R (1981), were administered. Due to fatigue or lack of time, a minority of the subjects did not complete all test conditions. We thus do not have the full four-scale IQ measures of 3 subjects. The digit span test was included in the study only after initial testing of nine subjects, and was thus not administered to these 9. Norwegian norms for the WASI and WAIS-R are still not developed, but the tests have for quite some time been widely used by Norwegian researchers with the American norms. Our choice fell upon

the WASI because this was the only known test of fluid and crystallized intelligence with norms up to 89 years of age. As a screening for dementia, we used a cut off IQ score of 75, and all participants satisfied this criterion.

### ERP stimuli

We applied an auditory oddball paradigm, with .20 target tones probability. The subject's task was to discriminate an 80 dB 80ms duration target tone of 1200 Hz from an 80 dB 80 ms standard tone of 750 Hz, and silently count the number of target tones. Inter-stimulus interval (ISI) was set to 1.5 sec., and 48 targets and 192 standard tones were administered in a random sequence. The tones had a rise/ fall time of 10 ms, and were presented through insert earphones calibrated to fit the stimulus presentation system. Before recording, an example of the task with 25 stimuli in a mixed sequence was presented. This procedure was adopted to ascertain all participants could easily discriminate target from standard tones, and to prime the subjects for the task. The subjects were asked whether they found it difficult to discriminate between the target and standard tones, and all indicated that they could easily hear the difference. In the actual task, subjects were asked to give the target count after completion of the presentation, and reported values were in the range 45-49. A simple factorial ANOVA showed no significant effects of age on number of incorrectly counted tones. The number of incorrectly counted tones in the ERP-paradigm did not correlate significantly with any other measure.

The specific target probability, intensity, frequency, tone duration and ISI were chosen in accordance with the recommendations from Polich's (1996) meta-analysis of aging effects on P300. Tone frequencies were chosen so as to be below the range of common high frequency hearing loss in the older age groups, and ISI was set long enough to secure attention to all tones as well as to allow recovery from habituation effects.

### ERP procedures

Subjects were seated in a chair within a sound attenuating recording chamber. The electrodes were placed in accordance with the international 10-20-system. A total of 14 electrodes (Ag/ AgCl) were used for recording; F7, F3, Fz, F8, F4, T3, C3, Cz, C4, T4, P3, Pz, P4, and Oz, referred to the left mastoid. A VEOG channel was obtained by placing one electrode above and one below the left eye, and ground was placed anteriorly. Inter-electrode impedance was generally measured to be less than 10 kOhm. For the recording of EEG activity, A/D rate was 500 Hz, and filter-setting was 0.10 Hz (high pass) and 70 Hz (low pass). In addition, a 50 Hz notch filter was applied. The signals were amplified by a

SynAmp DC amplifier (Neuroscan Inc.). Epochs were rejected from averaging if amplitude exceeded +/- 110 micro Volt, and eye blinks were corrected for statistically in accordance with Semlitsch et al.'s (1986) recommendations. Averaging was performed for target and standard separately. EEG was segmented in epochs of 900 ms duration (-100 ms to 800 ms relative to stimulus onset). All data average files were digitally filtered (30 Hz low pass) and baseline corrected before statistical measures of component latency or amplitude were made. Neuroscan software was used to present stimuli, record, and analyze EEG-activity.

### Data analyses

#### *ERP measures*

A computer program developed in our lab (Nielsen 1997) was used for the determination of peaks, defined as the most positive or negative point within a certain time domain relative to prestimulus baseline. In addition, the slope of the curve at the same time had to be equal to zero, thereby constituting a peak. That is, the peaks were determined algorithmically, in accordance with Pfefferbaum et al.'s (1990) recommendations. The P300 component was, for each electrode, set to the maximum positive point between 250 and 550 ms.

#### *Statistical analyses*

We correlated age with amplitudes and latencies for all electrodes in order to investigate whether any area of the brain is more prone to effects of aging than others. In addition, analyses of regression were performed and scattergrams presented to visualize the distributions of individual data points. We performed principal component factor analyses for amplitude and latency separately to investigate the possibility of inter-component clustering of amplitude and latency. The resulting factors were correlated with age for the purpose of investigating the association between age and the electrophysiological recordings from the various scalp areas, and with the neuropsychological measures. The purpose of these analyses was to index the relationship between the activity of different brain areas and performance on cognitive tests. In order to measure the relative potency of the neural generators at specific scalp locations, we performed correlation analyses, yielding an expression of the association between component amplitude and latency for each electrode. These analyses were performed for each of the five age groups. For the sample as a whole, we employed partial correlations to eliminate the age effect on the amplitude/latency relationship. Finally, we tested the linearity/curvilinearity of the relationship between age and the P300 component for each electrode by using both

age and age square in the analyses of regression. The results for Pz have been reported elsewhere (Walhovd and Fjell 2001), so here we focus on the pattern across other areas of the scalp.

## Results

### Effects of age on P300-topography

Grand average ERPs for target tones for each age group is shown in figure 1, and difference waveforms for Fz, Cz, and Pz, are shown in figure 2. The pattern of activation within the P300 time window for each age group separately is shown in figure 3. Correlation coefficients for age and P300 latency and age and P300 amplitude are shown in figure 4, and scatter plots with regression equations are shown in figure 5 and 6. The mean P300 latency and amplitude for each of the five age groups are shown in table I.

The age-latency correlations were stronger over posterior relative to frontal areas, and stronger at central relative to lateral sites (figure 4). The strongest correlations were found at electrodes Pz, P4, Cz, and Oz. Ten electrodes correlated significantly ( $p < .05$ ) with age, and the only electrodes that did not show a significant positive relationship with age were the lateral frontal electrodes F7, F4, F8, and the right temporal electrode T4. That is, four out of five correlations for the left hemisphere were significant, while only two out of five for the right hemisphere were significant. Overall, the pattern of correlations between age and amplitude resembled that of age and latency. Eight electrodes showed significant correlations, and here too, the strongest correlations were found at the posterior and central sites, with Pz, P4, Cz, P3, and Oz showing the highest values. All significant correlations, but one, were negative. The one exception was a positive correlation between F7 and age. These analyses were also done for males and females separately, but the pattern did not change in any substantial manner.

With age, the activity was more evenly distributed across the scalp, as evident in figure 3. As can be seen here, for the younger groups, the amplitude measures differ widely depending on the recording site, while the activation is much less varied across electrodes in the older groups. For all age groups, there is considerable less variation in latency than in amplitude across the different recording sites.

### Superordinate structures

A minimum of five subjects for each variable in factor analysis has been recommended (Zuckerman et al. 1988). Our sample size satisfies this criterion and allows the use of all 14 electrodes in the analysis. We applied factor analyses with varimax rotation at the level of elec-

trodes, and found that a four-factor solution fit the data of both latency and amplitude. This is in accordance with both the Kaiser-Guttman criterion of eigenvalues exceeding 1, and the number of factors representing the break point of the scree plot graph (Cattell 1978). Four factors yielded a cumulated explained variance for latency and amplitude of 74.8 and 87.7, respectively. The results of the factor analyses are shown in figure 7.

The four latency-factors were composed of Pz, Oz, P3, and P4 (factor 1), Fz, Cz, C3, and C4 (factor 2), F7, F3, and T3 (factor 3), and F8, F4, and T4 (factor 4). The four amplitude factors were composed of Pz, Cz, Fz, C3, C4, P3 and P4 (factor 1), F8, F4, and T4 (factor 2), F7, F3, and T3 (factor 3), and Oz (factor 4). While the fronto-temporal factors for both latency and amplitude were composed of the same electrode sites, the amplitude analysis yielded a larger fronto-temporal factor covering seven recording sites. In the latency analysis, this factor was split between central and parietal lines into two factors, each covering 4 electrodes. Each factor was then correlated with age (table II).

The latency parietal factor (factor 1) and fronto-central factor (factor 2) both correlated significantly with age, while the fronto-lateral factors did not. The only amplitude factor that correlated negatively and significantly with age was the big «fronto-central-parietal» factor. There was a significant *positive* correlation between the left fronto-temporal factor 3 and age.

### Neural generators

Figure 8 illustrates the search for neural generators by means of amplitude-latency correlations. The strongest associations were found at the right fronto-temporal recording sites. All the electrodes of the parietal line showed significant and negative amplitude-latency correlations, as did four out of five electrodes of the frontal line, in addition to T4. Amplitude and latency were negatively correlated for all electrodes

### P300-topography, neuropsychological measures, and aging

Table II shows correlations between the factors extracted by the principal components analyses and neuropsychological tests. The fronto-central latency-factor correlated negatively with digit span, block design, and matrices. These results indicate that a fronto-centrally based neurological generator of ERP components may also be involved in short-term memory and performance tasks. The left fronto-temporal factor correlated significantly with digit span. The right fronto-temporal factor and the parieto-occipital factor did not correlate significantly with any of the cognitive tests. For the amplitude factors, much of the same tendency was seen, with significant, positive correlations

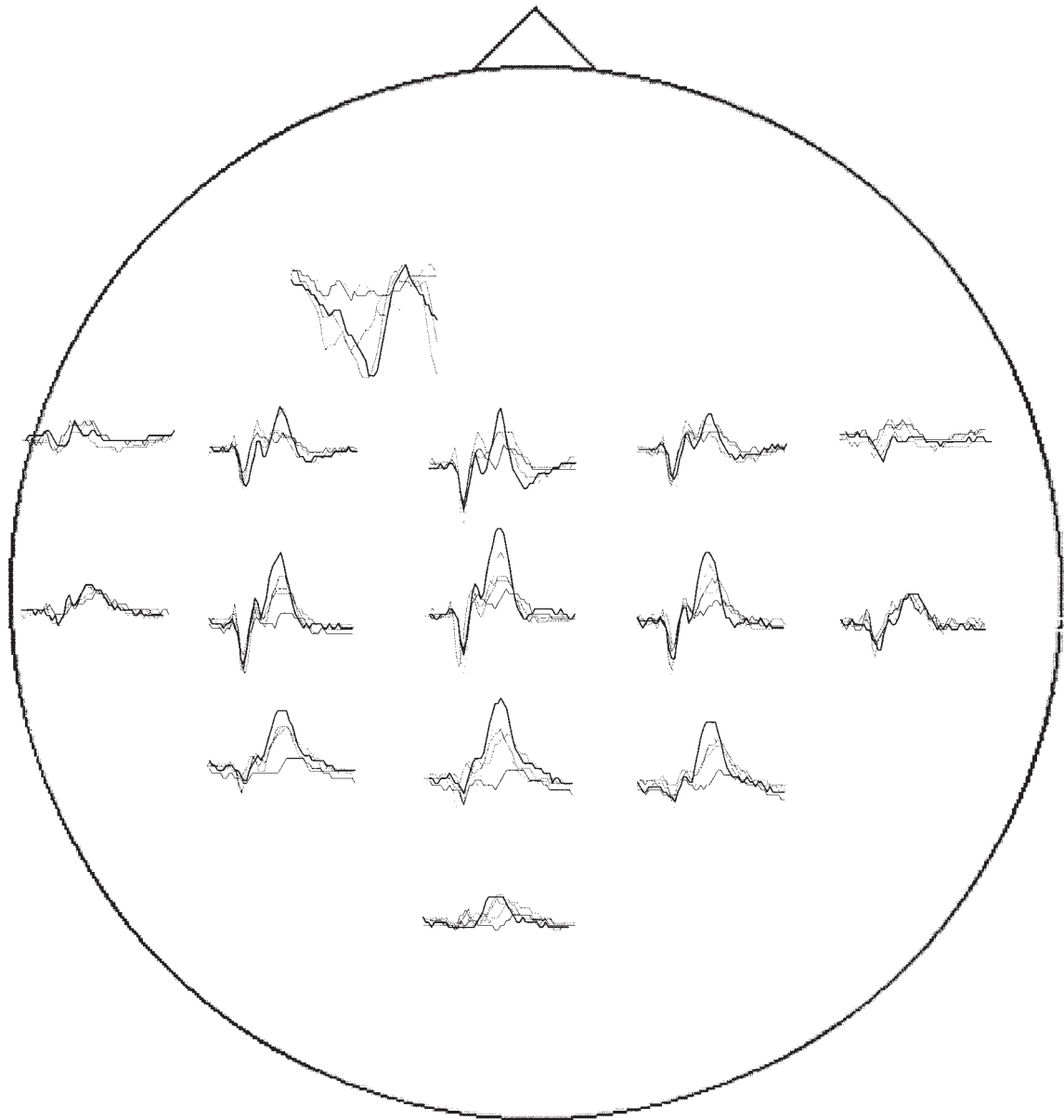


Figure 1. Grand average ERPs for target tones for each age group. Bold solid line: 20-34 years, Solid line: 80-94 years, Dashed line: 35-49 years, Dashed and dotted line: 65-79 years, Dotted line: 50-64 years.

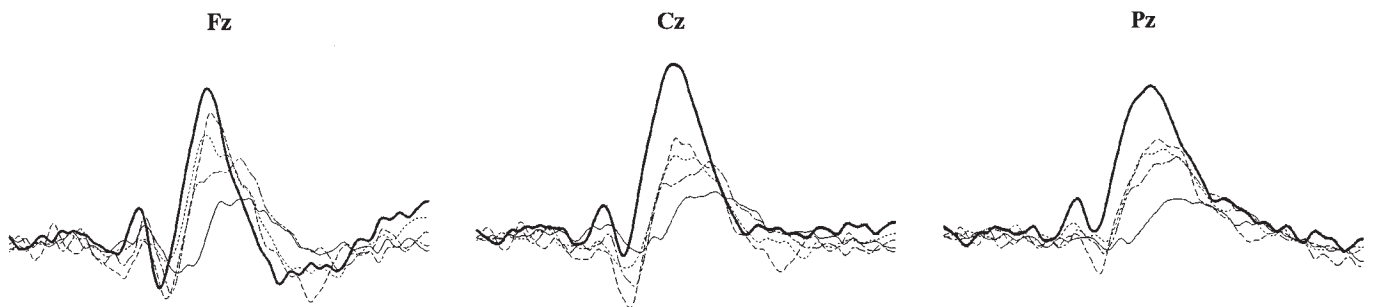


Figure 2. Grand average difference waveforms were derived by subtracting the standard tone event related potentials (ERPs) from the target tone ERPs. Waveforms are shown for Fz, Cz, and Pz for all groups. Group 1 (Bold solid line): 20-34 years, Group 2 (Dashed line): 35-49 years, Group 3 (Dotted line): 50-64 years, Group 4 (Dashed and dotted line): 65-79 years, Group 5 (Solid line): 80-95 years

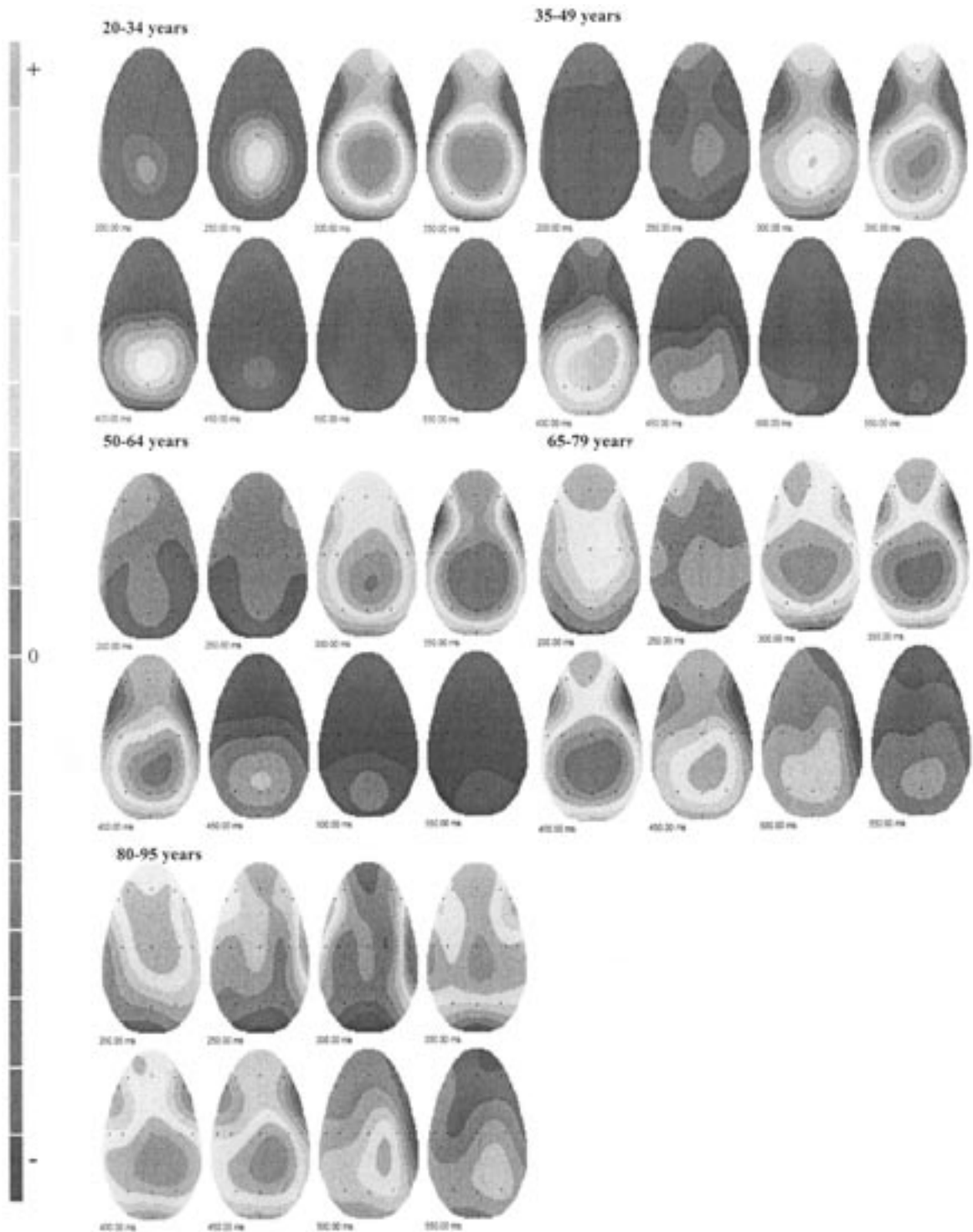


Figure 3. Two-dimensional presentation of topographic distribution of ERP activity in the P300 window in each of the five age groups. The presentation shows the distribution of activity across the scalp at each 50 millisecond from 200 to 550 ms after stimuli presentation for the target tones, separated by age groups. The presentation is rescaled: The most negative and the most positive amplitude value defines the top and the bottom of the scale for each age group. This means that the colour code represents the activity relative to the maximum/ minimum amplitude for the given age group. That is, for the oldest age group, the scale is much more narrow than for the youngest group. The presentation shows that the activity pattern in the older age group is more evenly distributed across the P300 time window than the activity of the younger age groups. The amplitude is very low in the youngest group, both before and after the P300 component reaches its peak while the activation is substantially higher in the older age groups.

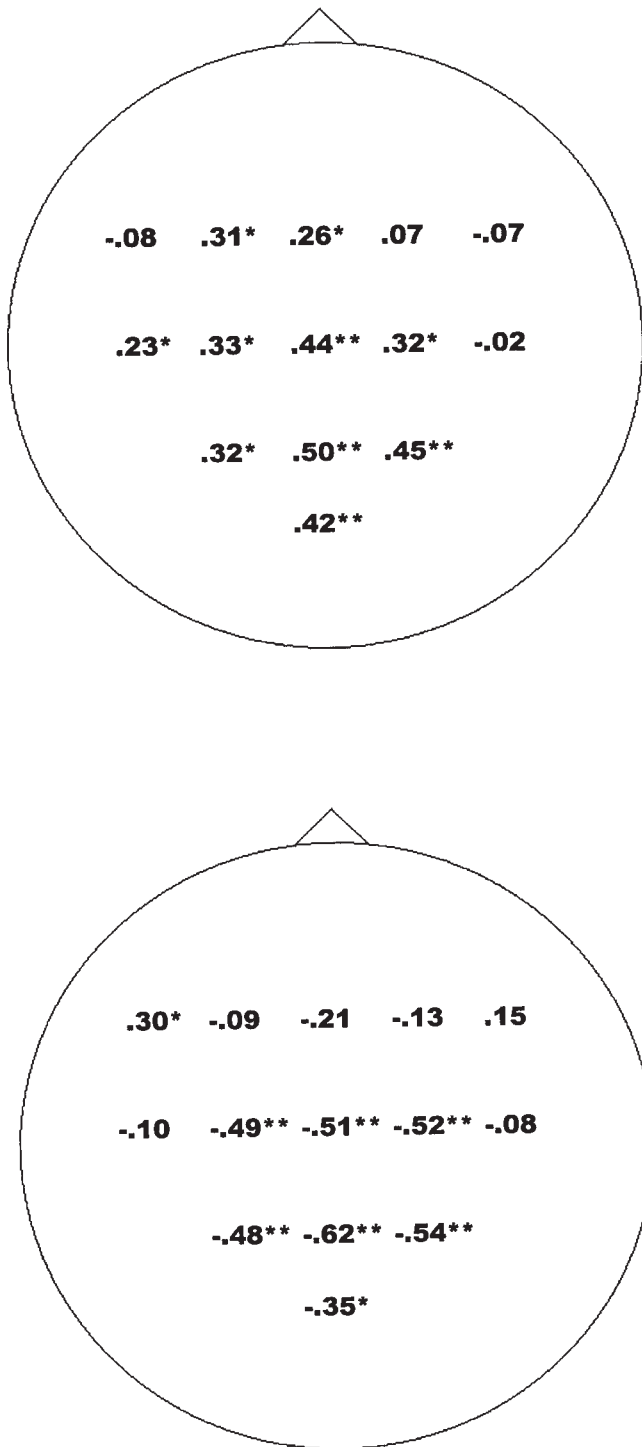


Figure 4. Correlation coefficients for age and P300 latency (top) and amplitude (bottom). \*  $p < .05$  \*\*  $p < .001$ .

between the fronto-central-parietal factor and digit span, block design, and matrices. The analysis also yielded a significant correlation between the occipital factor and

digit span forward. Finally, the left fronto-temporal factor correlated negatively with digit span forward and block design.

### Curvilinearity in aging

Our test of curvilinearity yielded only two significant curvilinear relationships; the regression line for Fz amplitude on age may be expressed by the formula  $y = 2.469 + 0.277x - .003x^2$ ,  $p < .05$ ; and the regression line for T3 latency on age may be expressed by the formula  $y = 400 - 3.298x + .034x^2$ ,  $p < .05$ . Based on our data, it may be concluded that a curvilinear expression generally does not explain the aging effect on the ERP component P300.

## Discussion

### Effects of age on P300-topography

The main effects of age on P300 latency and amplitude are illustrated in figure 4. In correspondence with previous studies, the strongest correlations with age were at central-parietal recording sites, i.e., Cz and Pz, somewhat less at Oz, with the weakest correlations at Fz and the lateral electrodes. Of much importance, however, is the increasing amplitude at the left fronto-lateral electrode F7, which demonstrated a positive correlation with age. This effect was not seen for any other electrode. The result is probably not caused by outliers in the material, as can be seen in figure 6. Although amplitude at the frontal recording sites generally does not correlate with age, it may be wise to interpret this single correlation with caution.

A popular interpretation of this general tendency for the frontal sites not to decline in activation with increasing age, is based on theories of frontal malfunctions in aging (Balota et al. 2000; Lowe and Rabbitt 1997; Vesco et al. 1993), partly founded on the reported neuronal loss in the frontal cortex of elderly persons (Lezak 1995; Parkin 1997; Woodruff-Pak 1997). As argued above it is likely that the observed variance in the pattern of recorded scalp electrical activation depends more on alterations of a functional character than on gross alterations of brain structures. A plausible explanation would then be that the elderly need more trials to build templates of the target stimuli, and hence experience the target stimuli as «new» stimuli for more trials. This, in turn, will make the task of counting the target stimuli, but not the standard stimuli, one involving greater demands on cognitive capacities, including selective attention and working memory, since the building of the target templates is not completed for a larger proportion of the session. These processes will depend more on frontally based control systems, and this may explain the relatively stronger activation observed in the frontal areas in terms

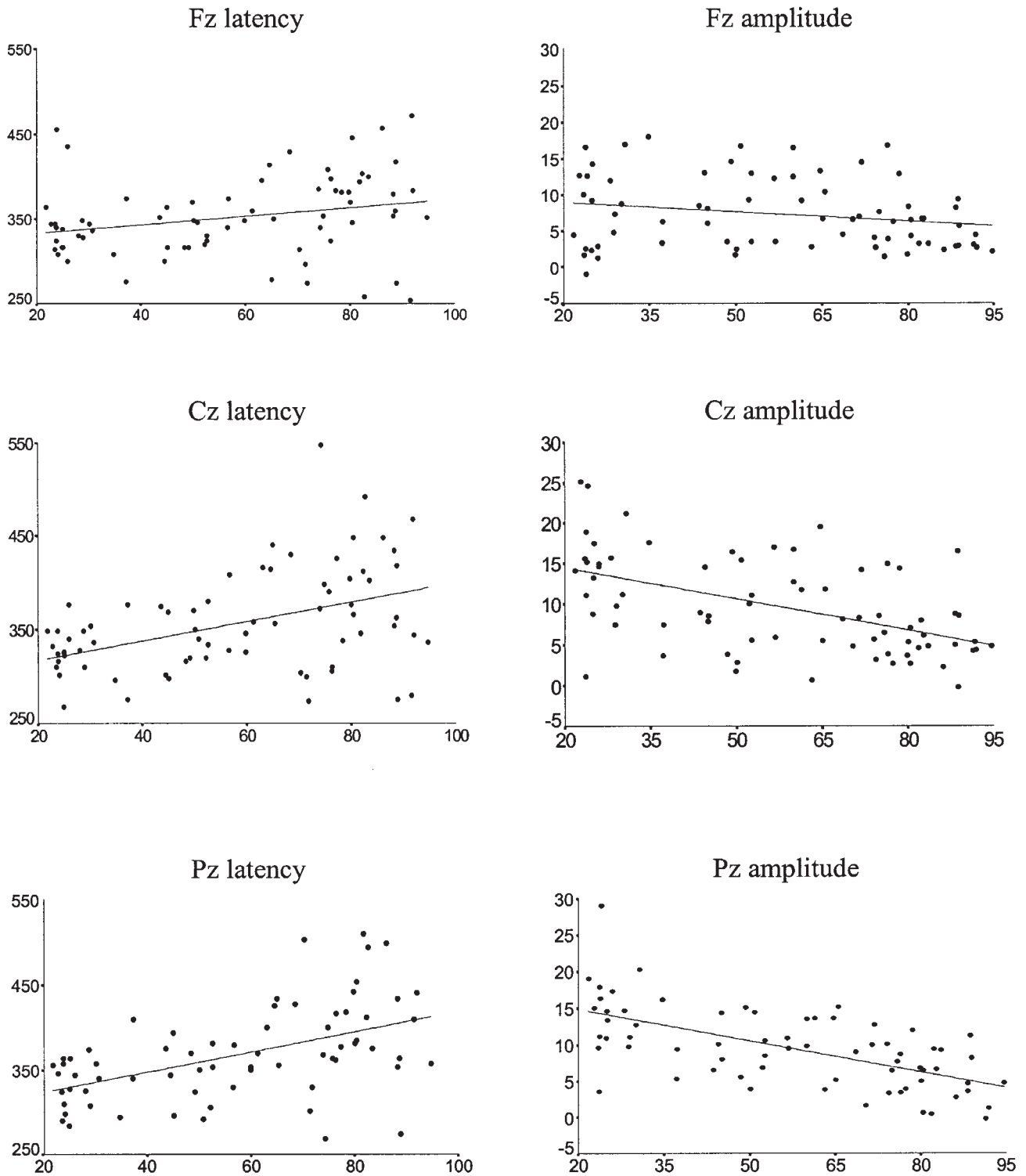


Figure 5. Relationship between P300 latency and age, and P300 amplitude and age, expressed in terms of regression equations, with respect to both linear and curvilinear relationships. Midline electrodes, Fz, Cz, and Pz, are presented. Fz latency:  $y = 323 + 0.05x$ , no significant curvilinear relationship found, Fz amplitude:  $y = 9.86 - 0.04x$  /  $y = 2.47 + 0.28x - 0.003x^2$  (curvilinear), Cz latency:  $y = 296 + 1.0x$ , no significant curvilinear relationship found, Cz amplitude:  $y = 17.05 - 0.13x$ , no significant curvilinear relationship found, Pz amplitude:  $y = 300 + 1.19x$ , no significant curvilinear relationship found, Pz latency:  $y = 17.73 - 0.14x$ , no significant curvilinear relationship found.

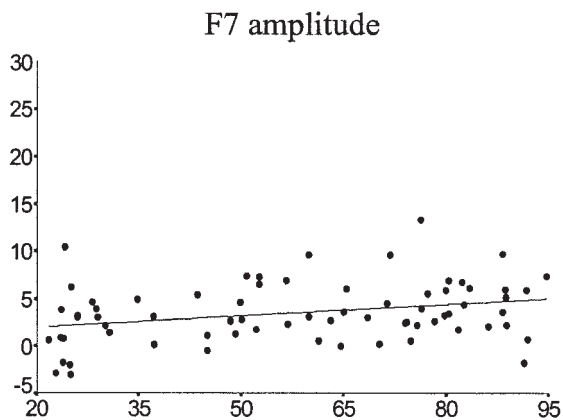


Figure 6. Relationship between P300 amplitude and age for F7, expressed in terms of regression equation. The P300 amplitude of F7 showed an interesting relationship with age. As can be seen from the figure, outliers in the material can hardly explain this relationship.  $y = 1.17 + 0.04x$ , no significant curvilinear relationship found.

of increased or maintained P300 amplitude. Based on this line of reasoning, one would expect the frontal activation to be maintained to a greater extent with increasing age, while the latency may simultaneously be delayed.

A question, though, is why the observed frontal atrophy in the elderly coexists with a relative increase in amplitude. This may indicate that neural generators underlying the electrophysiological activity measured at

the scalp do not depend on the brain areas undergoing the most profound neuronal loss. Otherwise one would expect a decrease in amplitude at the frontal scalp electrodes, and this is quite contrary to what is observed here. The cognitive processes that are engaged in the relatively easy counting task include sustained attention, simple stimulus discrimination, and memory updating. The latency and amplitude of the left frontal area correlate moderately with digit span, indicating that this area may be engaged in the sustained attention and memory updating required by the counting task. However, while the latency and amplitude measures exhibit nearly identical correlations with digit span, only amplitude correlate significantly with age, and this indicates that the digit span correlation may be unrelated to age prone processes. The neuronal mechanisms underlying the negative correlations between age and digit span, then, have to be located elsewhere in the brain. To approach this matter, one could focus on a correlation between a cognitive measure and the amplitude of the left frontal area, with a correlation not simultaneously existing for this cognitive measure and the latency of the same area. Block design shows this pattern, with a significant correlation with the amplitude of the left frontal area but not the latency. However, the increase in amplitude in this area with age, and the decline with age of performance on the task, yield correlation coefficients with a negative value, and there is no reason to expect a causal relationship between the two.

Table I. Mean P300 latency and P300 amplitude for each of the five age groups.

Electrode	Group 1 (20-34 years) (N=19)		Group 2 (35-49 years) (n=9)		Group 3 (50-64 years) (n=12)		Group 4 (65-79 years) (n=15)		Group 5 (80-95 years) (n=17)	
	Lat.	Amp.	Lat.	Amp.	Lat.	Amp.	Lat.	Amp.	Lat.	Amp.
F7	350	2.1	282	2.2	308	4.3	327	4.3	325	4.5
F3	326	5.9	302	4.5	335	6.7	353	6.0	369	4.4
Fz	342	8.3	332	7.3	354	9.6	353	7.2	372	4.9
F4	328	6.1	329	4.2	334	7.4	350	5.0	333	4.3
F8	356	2.2	364	2.3	327	4.5	340	3.3	341	3.3
T3	344	5.7	307	3.7	308	4.6	359	5.6	373	4.3
C3	332	11.5	340	5.9	351	8.0	367	6.7	382	4.5
Cz	323	14.6	333	8.1	360	10.8	373	7.8	386	5.8
C4	328	11.8	341	7.0	352	9.6	350	7.8	374	4.6
T4	346	6.0	329	4.7	336	6.1	352	4.9	340	5.0
P3	345	10.6	364	7.3	351	7.7	389	7.1	395	4.6
Pz	331	14.6	365	8.4	358	10.0	385	7.8	410	4.9
P4	335	10.6	379	6.8	360	7.3	378	6.3	419	3.9
Oz	349	6.2	392	5.5	383	3.7	395	3.9	434	5.0

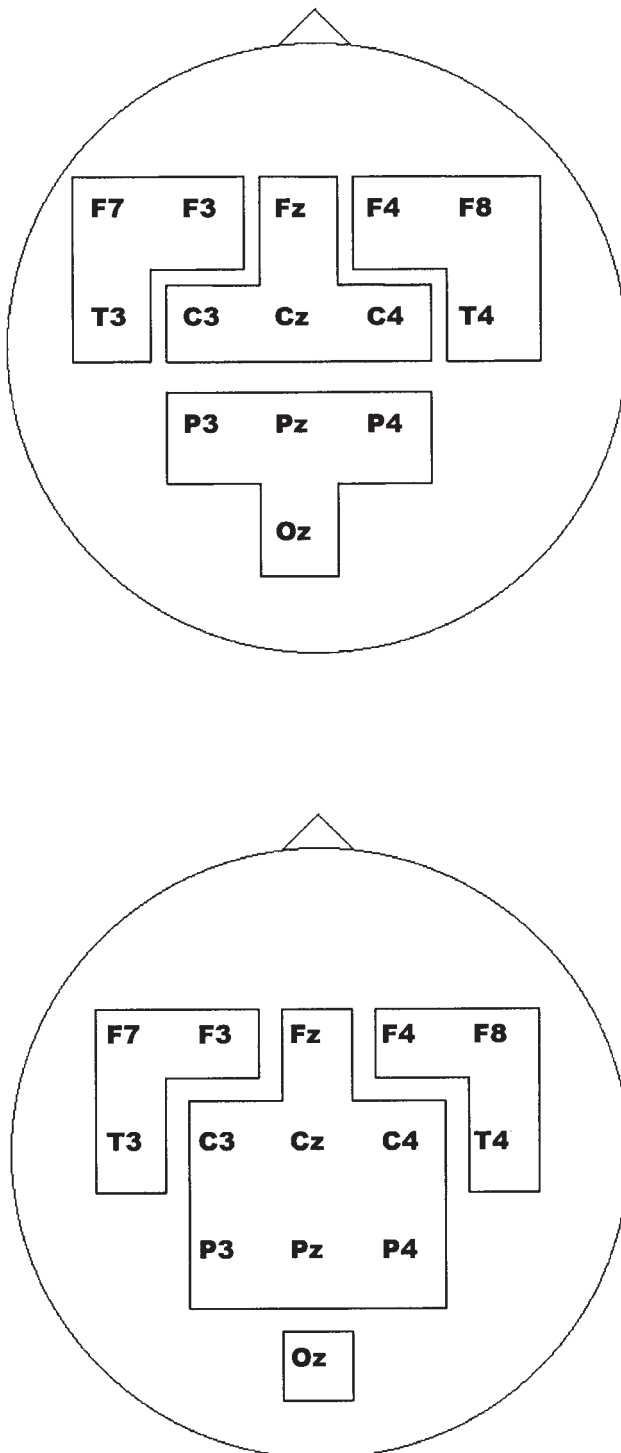


Figure 7. Varimax rotated principal component factor analyses of P300 latency (top) and amplitude (bottom). The boxes indicate how the activation patterns of the different electrodes cluster. Electrodes that tend to be activated in the same manner across individuals are placed in the same box. That is, the individuals who tend to have strong amplitude at Fz, will probably have strong amplitude on Cz as well. These analyses show areas of the scalp that with the same pattern of activation, in other words, the superordinate structures that exist in the material.

### Superordinate structures

As shown in figure 7, the factor analyses indicated that the left and the right fronto-lateral recording sites constituted separate factors for both amplitude and latency. The only one of these that correlated significantly with age was the left amplitude factor, with its positive correlation. The big fronto-central-parietal amplitude factor yielded a negative correlation with age of the same strength as the single electrode most associated with age. This indicates that the age-dependent variance is explained by this factor, and that a factor approach may be fruitful, as the reliability will increase with the number of recording sites. The latency factors were not identical to the amplitude factors. For latency, a division line between Cz and Pz emerged, yielding one parieto-occipital factor and one fronto-central factor. This indicates that the clustering of the electrodes is not identical for the amplitude and the latency measures, at least not in a population with great variations in age. Amplitude and latency may thus index partly independent aspects of processing.

### Neural generators

Figure 8 shows that for the sample as a whole, there were stronger partial amplitude/latency correlations for the right than for the left hemisphere. This finding gives support to Polich et al.'s (1997) observation of a pattern of stronger correlations over the right hemisphere. Apart from this, there were some differences in correlation patterns across age. In the youngest group, the strongest correlations were found at frontal recording sites, this corresponds to the findings of Polich et al. In the older groups, however, the strongest correlations were found more posteriorly. This anterior to posterior-shift in correlational strength were quite consistent across age groups. These results may imply that if Polich et al.'s assumption of the amplitude – latency correlation coefficients as an index of neuronal generator potency is correct, then the neuronal generators change with age. Fabiani and Friedman (1995) mention the possibility that the P300 source configuration in posterior and/or anterior brain regions is different in the elderly. This, however, may not be the most obvious conclusion. Alternatively, the amplitude and latency parameters recorded at each electrode could be partly independent measures of different aspects of the same or similar brain processes. This is seen for instance for the left frontal factor; here, amplitude correlates significantly with age while latency does not. The varying strength of each parameter's relationship with age may thus reflect that their relative importance in performance on different cognitive tasks change with increasing age. This would be consistent with Fabiani

Table II. Correlation coefficients for the four latency factors, the four amplitude factors and neuropsychological measures and aging.

Factors	Block design	Matrices	Digit span forward	Digit span backwards	Digit span total	Age
<b>Latency factors</b>						
Left fronto-temporal	-.12	-.21	-.19	-.29*	-.29*	.09
Right fronto-temporal	.15	.18	-.00	-.00	-.01	-.10
Parieto-occipital	-.16	-.23	-.15	-.14	-.16	.40**
Fronto-central	-.33*	-.34*	-.27*	-.17	-.28*	.30*
<b>Amplitude factors</b>						
Left fronto-temporal	-.29*	-.17	-.28*	.01	-.18	.24*
Right fronto-temporal	-.07	-.07	.10	.11	.17	.06
Fronto-central-parietal	.42**	.43**	.30*	.28*	.32*	-.61**
Occipital	-.05	.02	-.26*	-.07	-.18	.00

\*p<.05 \*\*p<.001

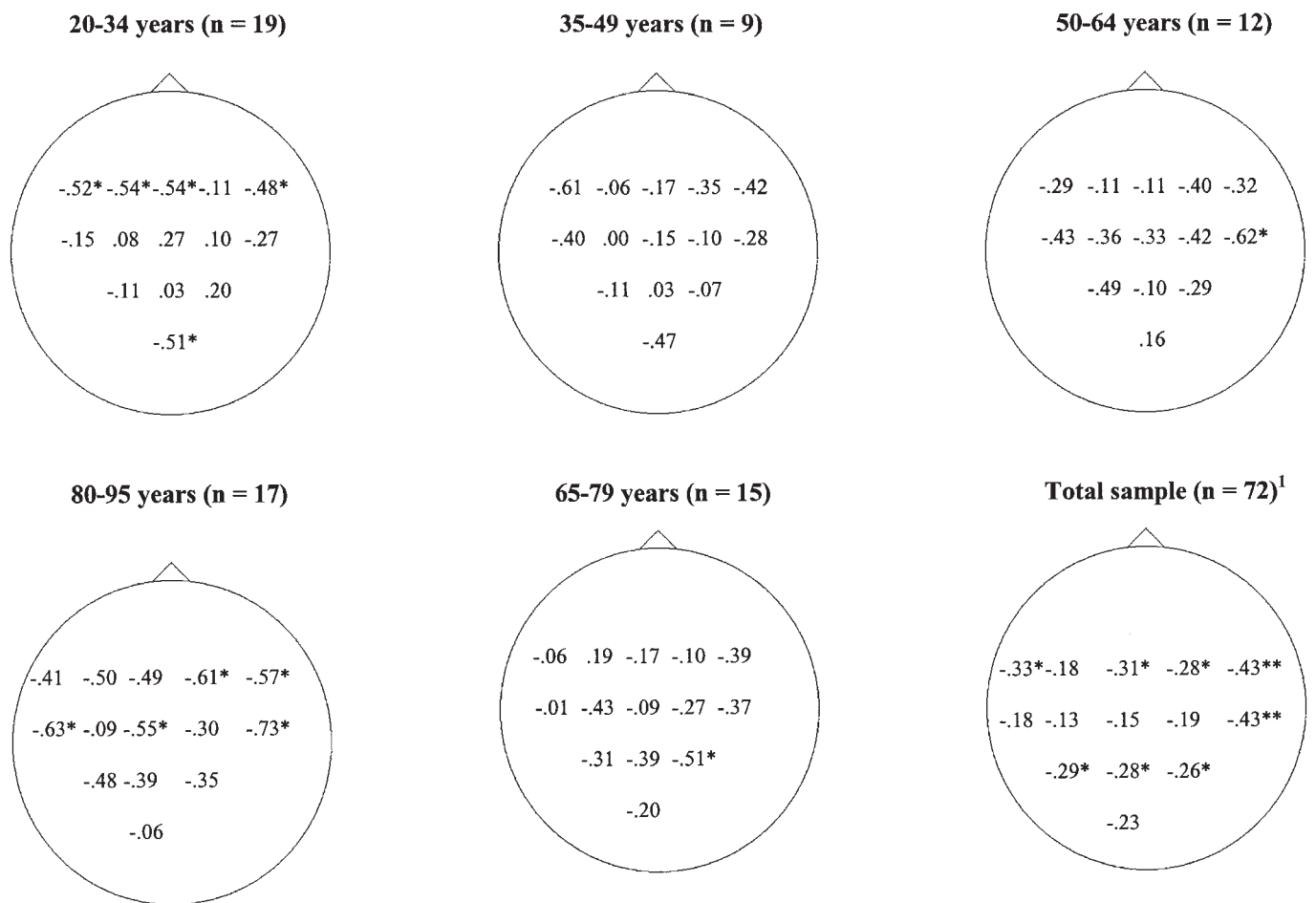


Figure 8. Correlations between P300 latency and amplitude for each age group and the total sample. The correlations for the sample as a whole are partial correlations, that is, the correlation coefficients express the age-independent relationship between P300 latency and amplitude. \* p < .05 \*\* p < .001

<sup>1</sup> Partial correlations, controlled for age

and Friedman's (1995) seemingly paradoxical suggestion that frontal neuronal loss could be functionally related to increased amplitude in aging.

#### P300-topography, neuropsychological measures, and aging

Table II shows that the neuropsychological measures correlate most strongly with the fronto-central-parietal amplitude factor and the fronto-central latency factor, that is, the central areas. The correlations are only moderate, however. Donchin et al. (1986) argues that P300 amplitude indexes brain actions stemming from maintenance of working memory. This interpretation fits our data neatly, and digit span was the single measure correlating with amplitude measures of most brain areas. Interestingly, there were no significant correlations between neuropsychological measures and the right frontal factor, neither for amplitude, nor for latency, but significant correlations with neuropsychological measures, mainly digit span, were found for the left frontal factor for both amplitude and latency. This may imply the existence of important topographical differences in the relationship between neuropsychological and electrophysiological measures. The tendency in our data, though, is that the two groups of measures clearly show the most evident association at the midline sites, especially the area covered by Cz and Fz, and their surrounding electrodes. This conclusion, however, has to be supported by data from a more homogeneous sample than ours, and possibly also by data based on a more extended battery of neuropsychological and cognitive tests than what is suitable with elderly subjects.

#### Curvilinearity in aging

We found a significant curvilinear relationship between age and electrical activity for only two electrodes, which were not even adjacent. It is hard to draw any strict conclusion from this, but the data seem to indicate that there is no reason to expect different answers to the linearity/curvilinearity question by analyses of different electrodes. There is a need for additional studies including more electrodes than the midline ones as well as high-density samples, so as to be able to address this question.

#### Concluding remarks

Our study, including a broader range of electrodes, support and expand previous findings indicating a more even distribution of the P300 component in aging. Our findings will necessarily imply that one has to consider age as a mediator variable when searching for neural generators of P300. Further, our findings point to the fact that one cannot speak of the relation between

electrophysiological and neuropsychological measures as a constant and fixed association, as the two seem not to be influenced by age in similar ways. A limitation to our study is the sample size. It would be preferable to correlate cognitive and neuropsychological measures within each age group separately, but the number of subjects studied is not large enough for this to be done properly. In order to accomplish this, we could define groups covering a larger portion of the age span. We do, however, feel that this would not be satisfactory, as there is such a considerable age variation with respect to the studied measures. Our study demonstrates the necessity of not exclusively studying homogeneous samples or only widely different groups, e.g., one young and one elderly. There is a need to include age as a continuous variable, and study samples in which the full age span is represented, as our data point to continuous changes in aging.

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