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Multivariate Analysis of Somatosensory Evoked Potential Parameters in Normal Adults*

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Summary. Cervical and cortical somatosensory evoked potentials (SEP) to median nerve stimulation were recorded in 65 normal subjects. Absolute peak latencies and amplitudes of cervical components N9, P10, N11, N13, P17, and cortical components P16, N20, P25, and N35 were measured. By means of partial correlations the interdependency of SEP-features could be verified in addition to the well-known dependence on arm length and age. In certain respects our results replicate other studies finding significant correlations between age and latency of early SEP-components as well as inverse relations between age and cervical amplitudes. Further analysis disclosed high intercorrelations between the latencies and between the amplitudes of the cervical and cortical components also revealing a certain exceptional position of the positive wave P17. In contrast to an inverse relation of amplitude and latency of the cervical components there were positive correlations between the respective features in the cortical evoked response. The findings are discussed with regard to the current knowledge about the origins of the SEP-components.

Key words: Somatosensory evoked potential – Cervical and cortical components – Effect of arm length and age – Partial correlation between latencies and amplitudes – Normal adults

Zusammenfassung. Bei 65 Normalpersonen wurden nach Stimulation des N. medianus cervicale und corticale somatosensorisch evozierte Potentiale (SEP) abgeleitet und die Absolutwerte der Gipfellatenzen und Amplituden der cervicalen Komponenten N9, P10, N11, N13 und P17 sowie der corticalen Komponenten P16, N20, P25 und N35 ausgemessen.

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Mit Hilfe von Partialkorrelationen ließen sich außer bekannten Einflüssen von Armlänge und Alter auf die SEP-Merkmale auch Abhängigkeiten dieser Merkmale untereinander aufdecken. In gewisser Hinsicht bestätigen unsere Resultate die Ergebnisse anderer Untersuchungen, wonach signifikante Korrelationen zwischen Alter und Latenzen früher SEP-Komponenten und inverse Beziehungen zwischen Alter und cervicalen Amplituden bestehen.

Darüber hinaus ergaben sich hohe Interkorrelationen für die Latenzen und für die Amplituden der cervicalen und corticalen Komponenten; eine gewisse Sonderstellung nahm die positive Welle P17 ein. Im Gegensatz zu einer inversen Beziehung zwischen Amplituden und Latenzen bei den cervicalen Komponenten zeigte sich bei den cortical evozierten Potentialen eine positive Korrelation zwischen den entsprechenden Merkmalen. Die Befunde werden im Hinblick auf die derzeitige Kenntnis über die Entstehung der SEP-Komponenten diskutiert.

Introduction

Short-latency somatosensory evoked potential (SEP) components depend on physiological determinants of which arm length and age are the best known. The effect of these variables on the amplitudes, latencies, and latency differences of SEP components has been the subject of a number of recent studies (Lüders 1970; Matthews et al. 1974; Drechsler 1978; Dorfman and Bosley 1979; Desmedt and Cheron 1980; Hume et al. 1982; Strenge and Hedderich 1982; Lüders et al. 1983). By taking these factors into account, the interindividual variability of parameters of the SEP can be reduced and their diagnostic sensitivity substantially improved.

For optimal clinical application the SEP components have to be comprehensively analyzed and multiple measurements fully describing the waveform characteristics obtained. For valid interpretation of separate parameters, especially with regard to the diagnostic uses of differences and ratios of latencies and amplitudes (Hume and Cant 1981; Lüders et al. 1983), it is necessary to know the interdependencies of these different SEP features under normal conditions.

To date no systematic study has assessed these phenomena. Thus, it is the purpose of this study to remove the influences of arm length and age and then to analyze the interrelationship among various SEP parameters in normal subjects.

Subjects and Methods

Somatosensory evoked responses were investigated in 65 normal subjects (26 females and 39 males, aged 15–71 years, mean age 35 years) without history, signs, and symptoms of involvement of the central or peripheral nervous system.

The stimulus was a 0.2-ms square-wave current pulse at a rate of 1.5 Hz applied to the right median nerve at the wrist (surface electrode). The intensity was adjusted to produce a thumb twitch. For recording platinum-iridium needle electrodes were placed subcutaneously

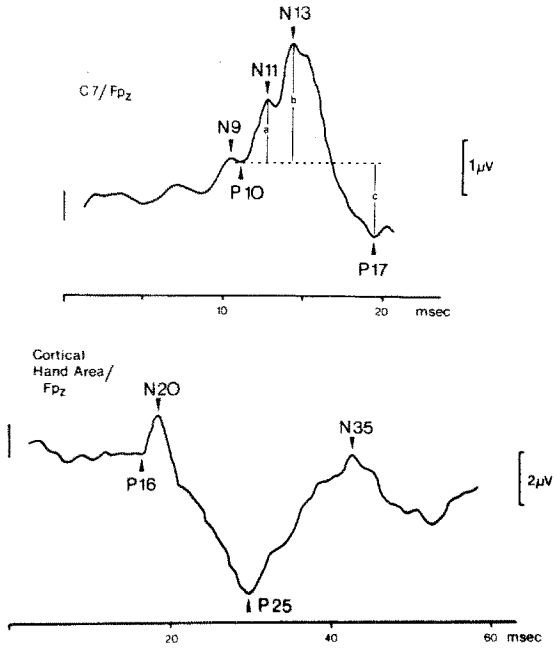

Fig. 1. Somatosensory evoked potentials to right median nerve stimulation recorded above the spinous process C_7 (*upper trace*) and over the cortical postcentral hand area C_3' (*lower trace*) using a midfrontal reference (Fp_z). *N* and *P* indicate the peaks of the investigated components. The cervical amplitudes are defined as shown in the figure (*a, b, c*). Both record negativity upwards.

between the spinal processes of C_6 and C_7 and on the scalp 2 cm posterior to C_3 and C_4 (C_3', C_4'), respectively, both with a common midfrontal reference electrode (Fp_z). The signals were recorded via an EMG amplifier (DISA 15 C 01; filter at 0.5-1000 Hz), averaged by a BIOMAC 1000 computer (256-1024 responses) and plotted by an X-Y pen plotter. The right arm was warmed by an automatically regulated infrared radiant heat to ensure a skin temperature of 36°–37° C along the median nerve trunk.

The arm length was measured as the distance between the wrist and the C_7 spinal process with the arm outstretched horizontally. Normal patterns of cervical and cortical evoked responses with a display of the parameters used in the study are shown in Fig. 1. Latencies were measured of the cervical N9, N11, and N13 potential components (Jones 1977) and of the cortical components N20, P25 and N35 (Goff et al. 1977). In addition, two positive deflections of the cervical response were considered, namely, the onset of N11, labelled P10 (Favale et al. 1982), and the positive wave following N13 whose first peak was labelled P17 (Strenge et al. 1981; Strenge and Hedderich 1982). For cortical response, the latency of positive peak P16 was determined, which corresponds to component P15 of other authors (Hume and Cant 1978; Mauguière and Courjon 1981).

Moreover, the amplitudes were analyzed of cervical N11, N13, and P17 (a, b, and c in Fig. 1) and the peak-to-peak amplitudes N13/P17 (b + c in Fig. 1) and cortical P16/N20, N20/P25 and P25/N35.

Both the latency and cervical amplitude data were approximately normally distributed. The data of the cortical amplitudes (x) were transformed ($\log x^2$). Intercorrelations (Pearson r) and partial correlations (e.g., Cooley and Lohnes 1971) were calculated from the values of all parameters.

SEP feature		Arm length (correlation coefficient r)
Latency	N 9	0.60
	P 10	0.69
	N11	0.77
	N13	0.71
	P 17	0.69
	P 16	0.51
	N20	0.65
Amplitude	P 17	−0.46

Table 1. Significant correlations between arm length and SEP-parameters ($P<0.001$)

Peak latency	Age	
	Correlation coefficient r	Partial correlation r_{xy} · arm length
N 9	0.29*	0.37**
P 10	0.32**	0.44***
N11	0.28*	0.43***
N13	0.41***	0.59***
P 17	0.26*	0.35**
P 16	0.23	0.26*
N20	0.40***	0.53***
P 25	0.05	0.05
N35	0.03	0.03

Significance of r values (two-tailed): *** $P<0.001$; ** $P<0.01$; * $P<0.05$

Table 2. Correlation coefficients and coefficients of partial correlation between age and latencies of SEP-components

Results

Relationship Between Arm Length and SEP Parameters

The correlations between arm length and various SEP parameters, which were significantly different from zero at the 0.001 level (two-tailed), are presented in Table 1. The parameters not related to arm length ($P>0.05$) are the latencies of cortical components P25 and N35, as well as all cervical and cortical amplitudes with the exception of the P17 amplitude, which showed a decrease with greater arm length.

Relationship Between Age and SEP Parameters

If diverse independent variables (e.g., arm length and age) have a simultaneous effect upon a dependent variable (in this case SEP parameters), the correlation between the dependent and one particular independent variable (age) can be ascertained more exactly when the influence of the other independent variable

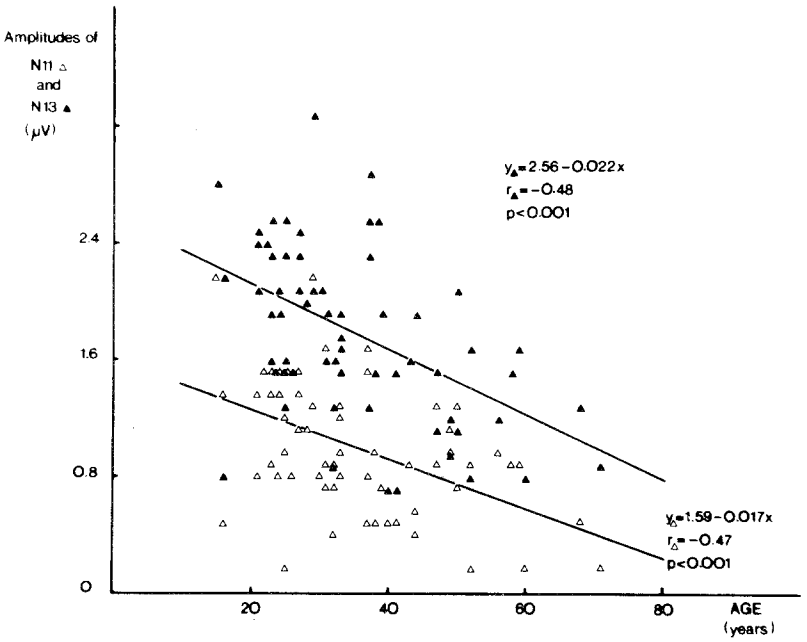

Fig. 2. Scatter diagram relating the amplitudes of the N11 and N13 components to the age. Separate regression lines have been drawn for each component.

(arm length) is removed. This can be done by calculating the coefficient of partial correlation. Correlation coefficients (r) and coefficients of partial correlation (r_{xy} · arm length) between age and SEP latencies are shown in Table 2. The interrelationship, i.e., the numerical value of the correlations, increased when the variance caused by the arm length was eliminated. A strong association between age and latencies was found for components N13 and N20; high correlations could also be verified for the latencies of P10 and N11 when the linear regression on arm length was removed.

There was a significant decrease ($P<0.001$) of amplitudes of N11 and N13 with age ($r=-0.47$ and -0.48, respectively). The results of the regression analysis can be seen in the scatter plot of Fig. 2. Only poor correlations ($P>0.05$) were calculated between the cortical amplitudes P16/N20, N20/P25, P25/N35 and age ($r=0.18$, 0.03, 0.01, respectively).

Relationship Between Various SEP Parameters (Partial Correlations)

Latencies versus Latencies. The interrelationships between the latencies of the cervical components and cortical P16 and N20 after removing the influence of arm length and age are summarized in Table 3. There was a strong association between most of the latencies; only the latency measures of N9 and P10 and the positive deflection P17 were not significantly related. Partial correlations between the latencies of the cortical components are listed in Table 4. The closest relationship was particularly found between adjacent components; there was an influence of N20 latency on all following latencies, whereas the preceding P16 component only correlated with N20.

Table 3. Partial correlation coefficients between different CEP and SEP latencies (effect of arm length and age eliminated)

Latency	N9	P10	N11	N13	P17	P16
P10	0.87***					
N11	0.79***	0.82***				
N13	0.67***	0.69***	0.72***			
P 17	0.19	0.17	0.36**	0.47***		
P 16	0.30*	0.46***	0.54***	0.53***	0.39**	
N20	0.35**	0.38**	0.53***	0.57***	0.39**	0.58***

Significance (two-tailed; DF=61): *** $P<0.001$; ** $P<0.01$; * $P<0.05$

Latency	P16	N20	P25
N20	0.58***		
P 25	0.21	0.51***	
N35	0.11	0.39**	0.76***

Significance (see Table 3).

Table 4. Partial correlation coefficients between cortical SEP latencies after removing the influence of arm length and age.

Amplitudes versus Amplitudes. The data of partial correlation between cervical amplitudes revealed a strong association only for the amplitudes of N11 and N13 ($r=0.65$; $P<0.001$), whereas the amplitude of P17 had no relationship to the N11 and N13 amplitudes ($r=0.06$ and 0.07, respectively; $P>0.05$). The cortical amplitudes of adjacent components showed significant positive correlations ($P<0.001$); P16/N20 vs. N20/P25: $r=0.59$; N20/P25 vs. P25/N35: $r=0.45$. The amplitudes P16/N20 and P25/N35 were not significantly related ($r=0.03$; $P>0.05$).

Latencies versus Amplitudes. Partial correlations between peak latencies and amplitudes of the cervical components N13 and P17 after removing the effect of arm length are summarized in Fig. 3. The correlation matrix represents the relationships among various parameters before (left side) and after (right side) additionally partialling out the influence of age.

There was a high correlation between the peak latencies of N13 and P17 ($r=0.56$; $P<0.001$), whereas the amplitudes of these components showed no dependency ($r=0.18$; $P>0.05$). The correlations between peak latencies and amplitudes were negative in all combinations (left side). Their numerical values decreased and in many cases lost statistical significance after the variance caused by age was eliminated (right side). Nevertheless, there was still a tendency toward an inverse relationship (negative values) between latencies and amplitudes. The relationships between the two latencies as well as between the amplitudes (top and bottom of the matrix) remained unchanged.

Partial correlations were also employed to determine the relationship among cervical wave amplitudes and latencies of early SEP components. The results are summarized in Table 5. The amplitudes of N11 and N13 were inversely related to

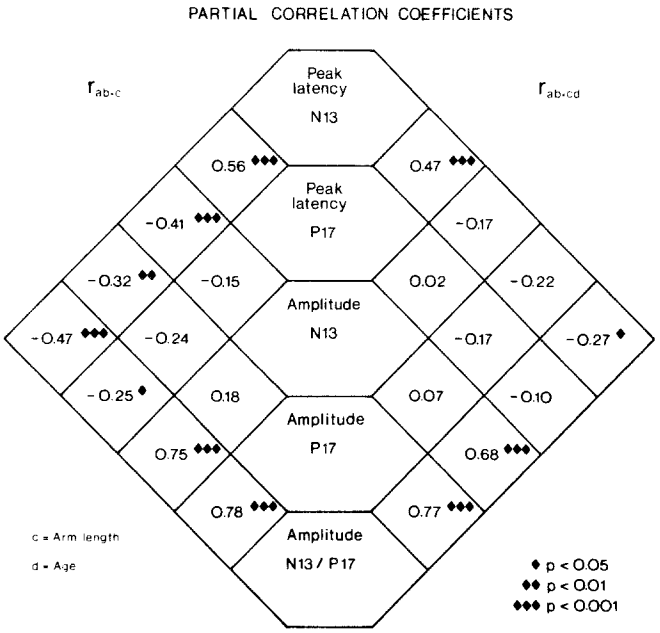

Fig. 3. Correlation matrix of partial correlations between various features of the cervical N13 and P17 components without the effect of arm length (*left*) and, in addition, without the influence of age (*right*)

Table 5. Partial correlation coefficients between cervical amplitudes and different SEP latencies (effect of arm length and age eliminated).

Latency	N9	P10	N11	N13	P17	P16	N20
Amplitude							
N11	−0.28*	−0.27*	0.02	−0.24	0.02	−0.05	0.08
N13	−0.26*	−0.23	−0.10	−0.17	0.02	−0.21	−0.25*
P 17	−0.04	−0.12	−0.17	−0.22	−0.17	0.17	−0.29*
N13/P17	−0.20	−0.24	−0.19	−0.27*	−0.10	−0.26*	−0.37**

Significance: ** $P<0.01$; * $P<0.05$

Table 6. Partial correlation coefficients between cortical amplitudes and latencies (without the effect of arm length and age)

Latency	P16	N20	P25	N35
Amplitude				
P 16/N20	−0.29**	0.20	0.21	0.15
N20/P25	−0.09	0.21	0.39**	0.36**
P 25/N35	−0.02	0.05	0.05	0.46***

Significance: *** $P<0.001$; ** $P<0.01$

the latencies of components N9 and P10. A similar relationship could be calculated between the amplitude of N13 and P17 and the peak latency of cortical N20. The peak-to-peak amplitude N13/P17 had significant negative correlations with the latencies of N13, P16, and N20.

The results of partial correlation analysis among latencies and amplitudes of cortical components are listed in Table 6. The data show a significant decrease in P16/N20 amplitude as P16 latency was increased. A stronger and positive relationship was found among the peak-to-peak amplitudes N20/P25 and P25/N35 and the latencies of P25 and N35, respectively. In addition, there was also a relatively strong association between N20/P25 and the following component N35.

Discussion

The present study confirmed the well-known dependence of peak latencies of early SEP components on arm length (Matthews et al. 1974; Hume and Cant 1978; Kritchevsky and Wiederholt 1978; Desmedt and Brunko 1980; Strenge et al. 1981). An unexpected finding was the statistically significant inverse relationship between the arm length and amplitude of P17.

In some respects, our data also replicate the findings of others with regard to the effects of age on the latency and amplitude of SEP components (Shagass and Schwartz 1965; Lüders 1970; Drechsler 1978; Dorfman and Bosley 1979; Desmedt and Cheron 1980; Hume et al. 1982; Allison et al. 1983). Generally, all cervical components showed prolonged latency and decreased amplitude in older subjects. A significant positive correlation with age was found for the latencies of cortical P16 and N20, whereas the components P25 and N35 were not significantly affected.

In view of these findings it is noteworthy that previous investigations concerning P25 and N35 contain some discrepancies as to the age-dependent changes. An unchanged latency of P1 (P25 in our study) and a significant shortening of latency N2 (corresponding to our N35) in older subjects were emphasized by Lüders (1970). Drechsler (1978), however, found a P1 latency increase and a significant prolongation of the left-sided N2 latency with age. A lack of age-dependent changes for the transit time from the onset of N20 to the peak of P25 was reported by Desmedt and Cheron (1980), offering a contrast to all other cortical time differences showing significant delays in aged subjects.

Cortical amplitude changes with age, in particular an increase, have been described by several authors (Lüders 1970; Drechsler 1978; Desmedt and Cheron 1980; Hume et al. 1982) but were not found in our study. However, it should be borne in mind that the present data were derived from a population with a different structure and a relatively limited range of ages in comparison to the studies mentioned above. In addition, there are indications of a nonlinear relationship between age and cortical amplitudes (Lüders 1970; Hume et al. 1982) which could have been masked by a possibly inappropriate linear function in this study.

As is evident from the partial correlations (Table 3), close relationships were consistently found for almost all cervical and early cortical latencies. The single exception was the lack of any association between the latency of P17 and those of components N9 and P10. The wave P17 has been shown to have properties similar to the P-wave in the spinal cord potential (Beall et al. 1977; Ganes 1982) related to presynaptic inhibition of the large-diameter afferent fibers (Schmidt

1971; Shimoji et al. 1975). The neuronal pathways for primary afferent depolarization have their own properties, with segmental as well as suprasegmental influences (Schmidt 1971). Thus, P17 cannot be regarded as a serial link in the somatosensory pathway, which is reflected by the chain of subsequent highly intercorrelated components, starting with N9 and P10 related to the peripheral nerve volley.

Close interrelationships were also found for the latencies of adjacent cortical components in accordance with the concept of a sequential synaptic activation of cortical generators. On this account, it is interesting to note that especially the wave N35 had rather strong associations with the earlier components in spite of some peculiar features decribed in previous studies (Larsson and Prevec 1970; Tsumoto et al. 1973).

By means of partial correlations it could be demonstrated that the inverse relations between latencies and amplitudes of N13 and P17 were mainly caused by the influence of age (Fig. 3). But after removing the variance associated with age a weak inverse relationship between latencies and amplitudes still remained, presumably related to a remaining influence of some kind of dispersion independent of age.

As is revealed by the partial correlations (Table 5), the peripheral conduction time (latency N9, P10) was inversely associated with the modal discharge of the dorsal horn synaptic pool (amplitude N13). Moreover, our data showed a close inverse relationship between amplitudes N13 and P17 and the latency of cortical N20. In our opinion, a non causal association on the basis of a common contributing factor (e.g., synchrony, temperature) could be a possible explanation for these phenomena.

In contrast to the inverse relationships between the cervical amplitudes and the latencies of early SEP components, the interrelation among the respective features of the components with cortical generators were characterized by positive partial correlations (Table 6). On this account, it seems worthwhile to point to the fact that the successive cortical SEP components presumably reflect sequential synaptic activities elicited by distinct cortical generators (Desmedt and Brunko 1980). However, there is a more or less overlap in time concerning these different activities with considerable influence on the wave form of the evoked potential (Desmedt and Cheron 1980). It is therefore tempting to consider an increase of cortical latencies as a spread of the cortical response leading to an enlargement of individual components with less mutual overlap and enhanced amplitudes.

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