Origin of P16 median nerve SEP component identified by dipole source analysis – subthalamic or within the thalamo-cortical radiation?

Abstract Following median nerve stimulation, several monophasic peaks were recorded at the scalp in the 15–18 ms time range. Source analysis, using three different methods, modelled a source near the centre of the head with an orientation towards the activated hemisphere and a peak activity at 16 ms post stimulus. Magnetic recordings detected no signal in this time range, which confirmed a subcortical location of the source. From dipole localization it was not possible to assign the exact origin of the P16 source to either the subthalamic level or the thalamo-cortical radiation, because of the limited spatial resolution at the centre of the spherical head model. An estimate of the conduction velocity of the medial lemniscus pointed towards a subthalamic origin. The P16 source was preserved in two patients with a lesion of the thalamo-cortical radiation and the ventral thalamus. Further evidence for a subthalamic location of P16 was derived from the physical mechanisms generating far-field potentials.

Key words Early SEPs · P16 · Source analysis · Human

Introduction

Following median nerve stimulation, one to several monophasic positive potentials with a peak latency of 15–18 ms preceding the cortical potentials can be recorded at the scalp (Abbruzzese et al. 1978; Albe-Fessard et al. 1986; Eisen 1982; Stöhr and Riffel 1982). These peaks are enhanced in visibility when higher stimulus rates or post-hoc digital high-pass filtering at about 200 Hz are used (Eisen 1982; Emori et al. 1991; Maccabee et al. 1986). The sources of these potentials are considered to be located in deep cerebral structures because of their latency peaking between the P14 arising at the level of the brainstem and the N20 generated at the somatosensory cortex. However, there is still disagreement with respect to the exact location of the deep structures responsible for this activity, e.g. the thalamus. A variety of studies recorded potentials within or near the thalamus and at the scalp (Albe-Fessard et al. 1986; Celesia 1979; Fukushima et al. 1976; Katayama and Tsubukawa 1987; Tsuji et al. 1984). One might summarise their results as follows: (1) Activity within the thalamus was recorded using implanted electrodes. (2) Some studies suggest that additional activity arises from neighbouring structures – the lemniscus medialis or the thalamo-cortical radiation. (3) In addition, there is controversy as to whether the activity recorded within or near the thalamus can be seen at the scalp.

If potentials generated within deep brain structures can be recorded at the scalp, this must be due to an open field characteristic of the deep structure concerned (Lorente de No 1947; Nunez 1981). Hence, it is unlikely that potentials generated within the thalamus itself are recordable at the scalp (Arezzo et al. 1979). Local neuronal activity generating far-field potentials recordable at the surface of the volume conductor, the head, can be approximated by an equivalent dipole (Jewett et al. 1990; Nunez 1981). This makes it possible to determine these SEP generators by dipole modelling. Spatio-temporal dipole modelling explains fields within a given time range by overlapping activity of a restricted number of equivalent dipoles with stationary positions and orientations but time-varying amplitudes (Scherg 1990; Scherg and von Cramon 1985).

Dipole analysis of early SEPs provided a model of three major sources in good agreement with the physiology and anatomy of the somatosensory system (Buchner and Scherg 1991; Buchner et al. 1994ab; 1995; Franssen et al. 1992). The first equivalent dipole source is located...
in the region of the brainstem, peaks around 14 ms post stimulus and explains most of the scalp potential P14. The second dipole activity is located in the region of the somatosensory cortex very close and almost perpendicular to the posterior bank of the central sulcus. This source peaks around 20 ms post stimulus and explains the N20–P20 scalp potential field. The third dipole activity is also located in this region but is more superficial, peaks around 22 ms post stimulus and explains the P22 field at the scalp.

In a preceding preliminary study, our group had been able to demonstrate an additional source located near the centre of the head model, peaking between P14 and N20 (Buchner and Scherg 1991). The present investigation extends the former study using an improved technique of data acquisition and three different approaches of source analysis. The major aims of the present study were: (1) to evaluate the existence of a far-field recordable source at or near the thalamus and (2) to attribute this source to an anatomical structure.

**Methods**

**Subjects**

SEPs were recorded from 14 normal right-handed subjects, aged 22–42 years (nine men, five women). All subjects gave their informed consent. In addition, SEPs were recorded in two patients (a 68-year-old woman and a 70-year-old man) suffering from acute complete stroke in the territory of the median cerebral artery.

**SEP recording**

The median nerve at the right wrist was stimulated using constant-current-square wave pulses of 0.2 ms duration with a repetition rate of 4.7/s and an intensity of twice the motor threshold. SEPs were recorded from 33 scalp electrodes against a reference at Cz in nine subjects and in the two patients and from 65 electrodes in five subjects. In these latter subjects, the electrodes were placed at the mastoid and the inion and were placed more densely over the contralateral left hemisphere. SEPs were sampled with a bin width of 200 μs and a system bandpass of 5–1500 Hz. At least four replications of 1000 sweeps covering a period from 20 ms before stimulus to 40 ms post stimulus were averaged.

**SEF recording**

Median nerve somatosensory evoked magnetic fields (SEFs) were recorded in those five subjects who also had a 64-channel SEP recording. The stimulus and recording parameters of the magnetic measurement were identical to those used for the electrical recordings. The MEG system had an arrangement of 31 channels (first-order two-turn gradiometer, 20 mm diameter, 70 mm base length, outer diameter 132.5 mm). The overall system noise was below 10 fT/Hz^{1/2} (Dössel et al. 1993). Using multiple test measurements, the position of the MEG system relative to the head was adjusted in such a way that the tangential source around 20 ms latency (N20–P20) was located at its centre.

Measurement of electrode positions and best fit sphere

The actual positions of the electrodes in 32-channel recordings from normal subjects were measured following the SEP measurement using a mechanical arm with six degrees of freedom and a high-resolution incremental digitizer, while the head was fixed in a special clamp.

The actual positions of the electrodes in 64-channel recordings were obtained from 3D-MR tomograms (128 continuous slices, 1.56 mm thickness) obtained on the same day as the SEP. Electrode positions for the MR were marked by small, wooden, fat-filled discs. MRs were read into a computer-assisted surgery system (Adams et al. 1990; Buchner et al. 1994b). The X-Y-Z coordinates of the electrodes were assigned to each amplifier channel, read to file and transferred to a PC. A separate PC program was used to perform a least-square fit for the sphere best fitting the 3D electrode cloud. Finally, electrode positions were transformed into the spherical coordinate system of the BESA program, which was used for further analysis.

Electrode positions in patients were not measured. Instead, averaged positions from the normal subject group were used.

**Data pre-processing**

First, data were baseline corrected by subtracting the mean signal from –20 to 0 ms and signals between 0 and 30 ms post stimulus were transferred to the BESA program. Then, data were referenced to the average reference and digitally filtered (high pass: 20 Hz, 6 dB/oct forward filter; low pass: 825 Hz, 24 dB/oct, zero-phase-shift filter) in order to enhance the signal-to-noise ratio and to reduce the overlap of low-frequency EEG components. This overlap, if not filtered out, can lead to substantial dipole mislocation. Also, most of the energy of the early SEPs is contained in this frequency band (Lüders et al. 1983, 1986). In addition, high-pass filtering at 100 and 200 Hz (12 dB/oct zero-phase-shift filter) was performed.

**Source analysis**

A four-shell spherical head model was used to obtain an independent source model for each SEP data set (scalp thickness 6 mm, conductivity 0.33 Ω/m; bone thickness 7 mm, 0.0042 Ω/m; CSF thickness 1 mm, conductivity 1 Ω/m; brain conductivity 0.33 Ω/m).

Three different approaches were used: (1) a single moving dipole – location, orientation and magnitude of one equivalent dipole computed at each digitalisation point – fitted over the signal epoch from 10 ms to 30 ms post stimulus; (2) spatial imaging using an adaptation of the MUSIC method (Mosher et al. 1993) to the EEG as implemented in the BESA program; and (3) spatio-temporal multiple dipole source analysis (Scherg 1990).

Spatio-temporal source analysis was always started with one regional source, consisting of three orthogonal dipoles at one location representing the three-dimensional current flow within the surrounding brain region, fitted in the interval between the start of the P14 component at the inion and the start of the N20 component at electrode P3. Next, a second regional dipole source was added and fitted in the interval between the start of N20 and the next positive peak at electrode P3. Then, the orientation of the first dipole of each regional dipole source was rotated to explain the total current flow at the time of maximal activity of the regional source in its respective epoch. The third dipoles of each regional dipole source were switched off, because they consistently showed less than 10% of the activity of the maximal dipole after rotation. The orientation and location of the second regional dipole source were fitted during its epoch, and finally the location and orientation of the second dipole of the first regional dipole source were optimised in the total epoch. No optional constraints to the inverse procedure were used. The location, orientation and dipole moment, as well as the time point of the start and peak of each dipole source activity, were collected for further statistical evaluation.