High frequency oscillations in early cortical somatosensory evoked potentials

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Abstract

Objective: To evaluate the characteristics of high frequency (HF) components of the early cortical somatosensory evoked potentials (SEPs).

Methods: We recorded 8-channel SEPs from the frontal and left centro-parietal scalp after right median nerve stimulation with a wide band-pass (0.5-2000 Hz) and digitized at 40 kHz sampling rate in 12 healthy subjects. HF components were analyzed after digital band-pass filtering (300-1000 Hz). The power spectrum was obtained by a maximum entropy method.

Results: HF oscillations (maximum power at 600-800 Hz) consisting of 5 to 8 peaks were discriminated from the preceding P14 far-field in all cases and their phases were reversed between the frontal and contralateral parietal regions. In addition, in subjects with a high amplitude central P22 potential in original wide-band recordings, a single HF oscillation with a maximum at the central region was present. Furthermore, this component showed no phase reversal over the centro-parietal area.

Conclusion: We therefore conclude that HF oscillations are superimposed not only on the tangential N20-P20 but on the radial P22 potential, and are generated from both tangential (area 3b) and radial (area 1) current sources. © 1998 Elsevier Science Ireland Ltd. All rights reserved

Keywords: High frequency oscillation; Somatosensory evoked potential; Median nerve stimulation; Central P22 component; Power spectrum; Maximum entropy method

1. Introduction

Cortical somatosensory evoked potentials (SEPs) after median nerve stimulation include waves of various frequency range, as spontaneous EEG does. Recent studies on somatic evoked magnetic fields disclosed that the initial cortical response contains high frequency (HF) components at around 600 Hz (Curio et al., 1994; Hashimoto et al., 1996). Hashimoto et al. (1996) reported that these HF oscillations show a tangential dipolar pattern and that the estimated source of these activities is located in the primary somatosensory cortex (area 3b) very close to that of the N20m activity. The HF components in SEPs were originally described as small inflections superimposed on the N20 potential recorded from the contralateral parietal scalp using a wide-band filter (Cracco and Cracco, 1976; Abbruzzese et al., 1978). Although these components were discriminated as several high frequency peaks from the N20 response using an analog high-pass (Maccabee et al., 1983) or digital high-pass filtering (Eisen et al., 1984; Maccabee et al., 1986; Yamada et al., 1988; Emori et al., 1991), their tangential dipolar nature has not yet been clarified. The power spectrum of the HF components in scalp-recorded SEPs has not been determined, possibly due to the extremely low conductivity of the skull. In addition, it remains unknown whether the central P22 potential, suppo-
2. Subjects and methods

Twelve normal adults (9 men, 3 women) participated in the experiments. All were healthy university students. The mean age was 21.2 ± 2.3 years (range 19–27 years), and the mean height, 166.4 ± 5.5 cm (range 162–179 cm). The subject sat relaxed in a comfortable reclining chair in a quiet room that was air-conditioned and electrically shielded. During the recording session, the subject was encouraged to minimize muscle and eye blink interference and was kept awake. All the subjects gave their informed consent.

The right median nerve was stimulated at the wrist at the rate of 5 stimuli per second. Intensity was adjusted so as to induce a small muscular twitch in the thenar muscles. SEPs were recorded with thin subcutaneous needle electrodes (0.2 mm diameter) from the frontal scalp at Fz, the ipsilateral central scalp at C4, and 6 electrodes covering the left centro-parietal scalp at FC3 (3 cm anterior to C3), C3, CP3 (3 cm posterior to C3), and at the positions 2 cm medial to FC3, C3, or CP3 (see Fig. 1). The right ear served as a reference. Electrode impedance was maintained below 3 kΩ. The band-pass filter of the amplifier was set at 0.5–2000 Hz. Fifty ms SEPs (5 ms before stimuli) were digitized at a 40 kHz sampling rate (horizontal resolution; 25 μs per point). SEP components were labeled with positive (P) or negative (N) polarity and their modal peak latencies. For each run, about 1000 trials were averaged with a Dantec-Key Point electromyograph and 5 to 10 runs confirmed reproducibility. Data were stored on floppy discs and converted to IBM format for later off-line analysis.

For each subject, 5 to 10 sets of SEPs (5000 to 10000 trials) were averaged off-line to decrease baseline fluctuation or muscle artifacts. The wide-band (0.5–2000 Hz) recorded responses were digitally band-pass filtered (300–1000 Hz) to separate the high frequency oscillations from the underlying initial cortical response such as the N20 potential. The digital band-pass filtering, using Hamming window, was done with an operator length of 360 points (i.e. 9 ms) so that the postfiltered brain-stem P14 and cortical N20-P20 potentials were free from the stimulus artifacts. For each channel, the 2 ms recordings before and after the stimulus provided the zero baseline. The power spectrum of the high frequency responses was obtained by a maximum entropy method (Ulrych, 1972), allowing us to analyze the various periods of the records. An analysis period was usually between 5 and 30 ms after the stimulus, and the period of 15 to 30 ms was also chosen to eliminate the effects of P14 far-field. In some cases, the power of 700–800 Hz components with a 5 ms period was investigated at every 1 ms interval to demonstrate sequential changes in high frequency components (power spectral scanning).

Amplitude of P14 or N20 potential was measured from the baseline to the peak positivity or negativity in the wide-band recorded response at CP3 (channel 7 (Ch7)). P22 amplitude was also measured from the baseline to the peak positivity in wide-band recorded response at the central scalp (usually 2 cm medial to C3, Ch4). Amplitude of the high frequency peaks was determined as a mean value of the several measurements from the peak positivity to the following peak negativity in the digitally filtered tracings.

3. Results

3.1. High frequency components of far-field potentials and cortical N20-P20

The wide-band records included several notches or inflections on the ascending and descending slopes of the N20 peak in the contralateral parietal leads and those on the ascending and descending slopes of the P20 trough in the frontal leads. Small notches preceding P14 were P9, P11 and P13 far-field potentials, and they were all in phase in all leads. After digital high-pass filtering, these notches changed into oscillating waves with a high frequency range, which started at 8–9 ms after the stimulus and ended at 25–26 ms in all subjects studied. The original wave forms (the wide-band records) obtained from the 8 recording positions and the corresponding high-pass filtered ones (300–1000 Hz) in one subject are compared in Fig. 2. Similar to the frontal P20 and contralateral parietal N20, the frontal and contralateral parietal postfiltered waves showed an out of phase relationship (see also Fig. 3). In contrast, the HF components superimposed on the far-field potentials (P9, P11, P13 and P14) showed no phase reversal. On the basis of the above, HF oscillations overlying the initial cortical response were discriminated from the preceding P13–P14.
Fig. 2. The original SEPs (the wide-band recorded responses, left column) and digitally high-pass filtered (300–1000 Hz) SEPs (right column) to right median nerve stimulation in a 21-year-old woman (M.F.). The responses obtained from the 8 recording positions are shown in each row and those superimposed, at the bottom row. n indicates the number of the responses averaged. The right ear served as a reference. The stimulus rate was 5/s. Following the high frequency (HF) components of the P9, P11, P13 and P14 far-fields, cortical HF oscillations start at the onset of N20-P20 response around 16 ms and their phase reversal is clearly seen between the frontal (Ch1) or fronto-central (Ch2, Ch3) response and contralateral parietal one (Ch6, Ch7) (small gray arrows). In addition, at around 20 ms when the central P22 potential is dominant in wide-band recordings (Ch2-5), HF oscillations also are maximal at the central region (small black arrows). Note that a single HF oscillation overlying the central P22 (black arrow) is in phase in contrast to the phase reversed HF oscillations overlying parietal N20-frontal P20, suggesting a radial current source.

Far-fields in all subjects. HF components following the P13–P14 far-fields in the ipsilateral parietal lead were equivocal or absent (see the postfiltered trace of Ch8 in Fig. 2, right column). Cortical HF oscillations consisted of 5 to 8 negative peaks (mean ± SD, 6.2 ± 0.8) in the contralateral parietal leads and the same number of positive ones in the frontal leads. They started at the onset of parietal N20 or frontal P20 wave in wide-band recordings. However, in 3 cases, one HF peak was noted just before the N20-P20 onset.

3.2. Power spectral analysis

The power spectra of the original wide-band records and postfiltered high-frequency responses are compared in Fig. 4 (the same subject as in Fig. 2). The broad band spectrum (1–1500 Hz) of the original SEPs from 5 to 30 ms after the stimulus comprised two peaks of signal energy at 50–100 Hz and 500–800 Hz in this subject. The recordings from Fz (Ch1) and C4 (Ch8) showed the maximum signal power at less than 50 Hz. The results of the
other 11 subjects were similar. As to high frequency spectrum, the postfiltered SEPs between 5 and 30 ms after stimulation had the maximal signal power at around 650 Hz with a broad range of frequency between 400 Hz and 800 Hz. Those corresponding to the cortical responses (i.e. excluding the P9–P14 far-fields) in the contralateral parietal and central regions demonstrated a maximum peak or two within 700-800 Hz range, while the Fz and contralateral fronto-central leads showed the maximum signal power at 600–650 Hz in this subject (Fig. 4B). The power spectra of the contralateral parietal waves in the other 11 subjects are illustrated in Fig. 5. Although the patterns of the power spectra differed among the subjects, a significant power with 600–800 Hz range was consistent.

3.3. High frequency component of central P22

In 5 subjects who have a large amplitude central P22 potential in the original wide-band recorded traces, HF oscillation was also maximal in the central leads at the time when the P22 culminated (see Figs. 2 and 3A). In sharp contrast with the phase-reversal pattern of HF oscillations overlying the parietal N20-frontal P20, the HF oscillation superimposed on the central P22 showed a phase alignment (Figs. 2 and 3A, black arrows). A power spectral scanning at 1 ms interval of the parietal and central responses showed that time course of HF power in 700–800 Hz range differs for N20 and P22 responses (Fig. 4C). On the other hand, in subjects who showed equivocal or no P22 potential, only the phase-reversal pattern of HF oscillations overlying the parietal N20-frontal P20 was observed (see Fig. 3B).

The peak latencies and amplitudes of the P14, N20 and P22 components are summarized in Table 1.

4. Discussion

4.1. High frequency components of the far-field potentials and cortical N20-P20

Our aim in the present experiments was to assess a dipolar nature of the high frequency oscillations superimposed on the contralateral parietal N20 and frontal P20 potential after stimulation to the median nerve at the wrist. In order to minimize subcortical responses such as P9, P11, P13–14 or N18 potential, we used ear reference recording from multiple scalp sites. The P9, P11 and N18 potentials are also known to be canceled out in a routine practice using ear reference montage (Desmedt and Cheron, 1981). In fact, a widespread N18 potential was not discerned in the present experiments. However, because of an extensive averaging up to 10,000 trials, we obtained small P9 and P11 far-fields in addition to fairly large P13–14 potentials in the original wide-band traces, which result in clear HF oscillating waves by digital band-pass filtering. After superimposing the post-filtered traces, these HF components included in the far-field potentials turned out all in phase while cortical HF oscillations showed an out of phase relationship. Thus, we could confirm the dipolar nature of the HF components underlying the contralateral parietal N20 and frontal P20 wave. Superimposition of the contralateral parietal and frontal traces is reported to be a useful method in identifying the cortical N20-P20 response as a diverging wave in a routine wide-band recording (Ozaki et al., 1996a).

In previous work on digital filtering of the cortical SEPs, Eisen et al. (1984) failed to disclose the dipolar nature of the cortical HF components due to the use of the contralateral parietal scalp-to-Fz bipolar montage. Yamada et al. (1988) recorded SEPs, using ear reference, from the contralateral parietal and frontal scalp to describe 3 peaks at each region
just before the parietal N20 culmination. They did not, however, evaluate the HF components overlying the descending phase of parietal N20 potential. In accordance with the recent report on magnetically-recorded HF oscillations (Hashimoto et al., 1996), we have found that the cortical HF oscillations comprise 5 to 8 peaks showing a clear phase reversal between the contralateral parietal and frontal records.

4.2. Power spectral analysis

As to a broad band spectrum (1–1500 Hz) of the original SEPs, the signal energy of the contralateral parietal and central waves was maximum at 50–100 Hz while that of the records from Fz (Ch1) and C4 (Ch8) was at less than 50 Hz. Similarly, the signal power at higher frequency range obtained from the frontal scalp was slightly lower than that obtained from the parietal scalp in some subjects. A possible explanation for these facts is that the frontal electrode is located far from the generator source (area 3b) compared with the parietal electrode position.

A maximum entropy method which we employed has the advantage of an analysis period being optional and without 'edge effect' inherent in FFT analysis (Ulrych, 1972). When analyzing the poststimulus 5–30 ms for all traces, the HF power showed a wide range of frequencies due to inclusion of the far-field potentials such as P14. Therefore, we chose the analysis time of poststimulus 15–30 ms to obtain the cortical HF power, eliminating the influence of the far-fields. In addition, the maximum entropy method has the advantage that it provides a sharper peak of the dominant frequency power than the FFT analysis. In line with the previous reports on somatosensory magnetic fields (Curio et al., 1994; Hashimoto et al., 1996), HF power of the genuine cortical response consisted of 600–800 Hz range. In some subjects, however, the frequency power below 500 Hz was more dominant (Fig. 5, right column). Thus, considerable variation in cortical HF power may exist among individuals. Another possible explanation for this lower frequency power is that these subjects might have been sleepy in some sessions of recording though they were instructed to stay as alert as possible, because the amplitudes of HF components have been reported to decrease during sleep (Yamada et al., 1988; Hashimoto et al., 1996), and their signal energy shifts to lower frequencies (Hashimoto et al., 1996).

Fig. 4. Power spectral analysis of the SEPs to right median nerve stimulation in a 21-year-old woman (M.F.) (a maximum entropy method). (A) Broad band spectrum (1–1500 Hz) of the original recordings of 5–30 ms period. Two peaks are present at 50–100 Hz and 500–800 Hz, but the recordings from Fz and C4 show the maximum power at less than 50 Hz. Ordinate, relative signal energy power, arbitrary unit (rP(f)); abscissa, frequency. (B) High frequency band spectrum. Upper: the postfiltered SEPs from 5 to 30 ms after the stimulus including far-fields and early cortical responses. The signal power of all traces is maximum at 600–700 Hz. Lower: the postfiltered SEPs from 16.5 to 24 ms after the stimulus corresponding to early cortical responses. Thick line indicates the contralateral parietal lead (Ch7) and the dotted line, the central lead (Ch4), both of which include maximum power in 700–800 Hz range for the duration of the parietal N20 and central P22. The Fz and contralateral fronto-central leads show the maximum signal power at 600–650 Hz. (C) Sequential changes in 700–800 Hz power of the SEPs in the central lead (Ch4, upper) and in the contralateral parietal lead (Ch7, lower). Ordinate, relative signal energy power, arbitrary unit (rP(f)). Each line in the figure indicates the signal frequency power from 700 Hz to 800 Hz. Abscissa, poststimulus analysis period. For both Ch4 and Ch7, the 700–800 Hz frequency power for a 5 ms period was calculated with a maximum entropy method at every 1 ms interval from 6 to 25 ms after the stimulus. The 700–800 Hz power has a trough at 14 ms in both leads. The power in the contralateral parietal lead again culminates at 16–21 ms period when N20 reaches its peak whereas that in the central lead is maximal at 16–23 ms period, corresponding to P22.
4.3. High frequency component of central P22 potential

The central P22 potential is thought to reflect a radial current source from activation of primary somatomotor cortex, which may not contribute to scalp-recorded magnetic fields. The amplitude of that response is known to vary among individuals (Ozaki et al., 1996b). In 5 subjects, we could record a fairly large central P22 potential from the central and fronto-central leads in the original wide-band recordings. The postfiltered traces in the central and fronto-central leads showed that HF oscillations were also maximal at the time when the P22 culminated. In addition, HF oscillation superimposed on the central P22 showed a phase alignment, in sharp contrast to the phase-reversal pattern of those overlying the parietal N20-frontal P20. Furthermore, a power spectral scanning disclosed a different time course of HF power in 600–800 Hz range for N20 and P22. These results suggest that the HF oscillation overlying P22 potential cannot share the same generator as those superimposed on the N20-P20 potential (area 3b).

No previous studies have demonstrated the HF component confined to the central P22 response. There remains a debate about a generator source of the central P22 component. A possible candidate for generation of the P22 is the primary motor cortex (area 4) (Desmedt and Bourguet, 1985) or the primary sensory cortex (area 1) (Allison et al., 1989). The present findings favor the latter hypothesis since the HF oscillations are considered to reflect high-frequency spike bursts generated in the inhibitory interneurons of the primary somatosensory cortex (Steriade, 1978; Swadlow, 1989; Hashimoto et al., 1996).

In conclusion, we showed tangential dipolar nature of HF oscillations overlying the contralateral N20-frontal P20 response and radial dipolar nature of the HF oscillation superimposed on the central P22 potential. Analysis of the high frequency cortical responses may expand clinical application of SEPs in patients with various neurological diseases involving the somatosensory cortex.

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