

LOW-FREQUENCY OSCILLATIONS IN HUMAN TIBIAL SOMATOSENSORY EVOKED POTENTIALS

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ABSTRACT - Oscillatory cerebral electric activity has been related to sensorial and perceptual-cognitive functions. The aim of this work is to investigate low frequency oscillations (<300 Hz), particularly within the gamma band (30-110 Hz), during tibial stimulation. Twenty-one volunteers were subjected to 5 Hz stimulation by current pulses of 0.2 ms duration and the minimum intensity to provoke involuntary twitch. EEG signals without (spontaneously) and during stimulation were recorded at primary somatosensory area. A time-frequency analysis indicated the effect of the stimulus artifact in the somatosensory evoked potential (SEP) frequencies up to 5 ms after the stimulus. The oscillations up to 100 Hz presented the highest relative power contribution (approximately 99%) for the SEP and showed difference ($p < 0.01$) from the frequencies of the spontaneously EEG average. Moreover, the range 30-58 Hz was identified as the band with the highest contribution for the tibial SEP morphology ($p < 0.0001$).

KEY WORDS: gamma oscillations, somatosensory evoked potential, tibial nerve, time-frequency analysis.

Oscilações de baixa frequência no potencial evocado somato-sensitivo do nervo tibial humano

RESUMO - Oscilações da atividade elétrica cerebral têm sido associadas a funções sensoriais, de percepção e de cognição. O presente estudo objetiva investigar as oscilações de baixa frequência, em particular da banda gama (30-110 Hz), durante estimulação do nervo tibial. Vinte e um voluntários foram estimulados com pulsos de corrente de 0,2 ms, frequência de 5 Hz e intensidade mínima para produzir o movimento involuntário dos músculos intrínsecos do pé. Sinais EEG espontâneo e durante estimulação foram registrados na área somato-sensitiva primária. A análise tempo-frequência indicou o efeito do artefato ao estímulo na banda de frequência do potencial evocado somato-sensitivo (PESS) até aproximadamente 5 ms pós-estímulo. As oscilações até 100 Hz apresentaram maior contribuição relativa de potência ao PESS (aproximadamente 99%) e se mostraram significativamente diferentes ($p < 0,01$) das frequências da média coerente do EEG espontâneo. Além disso, a banda 30-58 Hz foi identificada como a de maior contribuição à morfologia do PESS do nervo tibial ($p < 0,0001$).

PALAVRAS-CHAVE: oscilações gama, potencial evocado somato-sensitivo, nervo tibial, análise tempo-frequência.

Oscillatory neural activity has been investigated at cellular level¹, in human electroencephalogram (EEG)² and magnetoencephalogram (MEG)^{3,4}. Such oscillations have been related to sensory processing^{5,6} and perceptual-cognitive functions^{7,8}. Various functional mechanisms have been associated with this phenomenon as: memory⁹, attention¹⁰, object representation¹¹ and pain perception¹². Thus, according with Basar et al.⁶, the brain oscillations should explain the binding problem between the sensory processing and cognitive functions.

EEG recordings have revealed the existence of

transient frequency oscillations in different bands, mainly in the gamma band (30-110 Hz). Several authors^{6,7,13,14} have pointed out that if these oscillations appear with the same latency and phase after each stimulus, then it is considered evoked activity. Moreover, different authors^{2,10,15,16} reported that these oscillations build up the morphology of the evoked potential (time average synchronized with the stimulus).

Evoked oscillations of high frequency (300-900 Hz) during somatosensory stimulation of tibial nerve have been investigated by several authors¹⁷⁻²⁰. The

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present study aims at investigating the brain oscillations in the frequency band up to 300 Hz, particularly within the gamma band, during stimulation of the right tibial nerve. In addition, the effect of the stimulus artifact in the evoked response is also estimated, both in time and frequency domain. For such investigation, the spectral analysis and statistical test will be applied to the somatosensory evoked potential (SEP).

METHOD

Subjects – EEG signals without (spontaneously) and during electrical stimulation of the right posterior tibial nerve at the ankle were recorded from twenty one volunteers (18 male), aged between 18 and 42 years old, and height from 1.55 to 1.86 m (Table 1), with no symptoms of neurological pathology and with normal SEP. The eyes of the subjects were closed during a state of relaxed wakefulness throughout the experiment. The SEP's were visually checked by an experienced clinician. The local ethics committee (CEP-HUCFF/UFRJ) approved this research.

Stimuli – The volunteers were subjected to periodic stimulation using a Sapphire[®] 4ME (Medelec, UK) Evoked Potential System and two Ag/AgCl electrodes (distance 3 cm). A ground electrode was placed at popliteal fossa. Current pulses of 0.2 ms duration and minimum intensity (5-24 mA, Table 1) to provoke the involuntary twitch (motor threshold - *MT*) of the intrinsic foot muscle supplied by the tibial nerve were employed. The stimulus rate was 5 Hz, for which clearly defined evoked responses are expected²¹. Two sessions of 1024 stimuli (*MT*₁ e *MT*₂) were carried out, with at least one minute interval between stimulation periods.

EEG signals – The recording electrodes (Ag/AgCl) were positioned at Cz' (2 cm behind the Cz electrode position

of the 10-20 International System), with the reference at Fpz' (midway between Fpz and Fz), as is usual for somatosensory evoked potentials²². The electrode impedance kept below 2 kΩ and the bandpass filter of the Evoked Potential System was set at 10 Hz to 2 kHz. The raw EEG signal from the analog output of the Sapphire[®] was digitized at a sampling rate of *f*_s=5 kHz and a resolution of 12 bits (DAQPad-1200, National Instruments, USA), using software developed in LabVIEW (Version 5.01, National Instruments, USA). The trigger signal, showing the instant of each stimulus, was also acquired. The environmental temperature was controlled nearly 25°C, that is 25.1±0.6°C.

Somatosensory evoked potentials (SEP) – The estimated SEP by coherence mean technique (time average synchronized with the stimulus) of *M*=800 epochs (epoch is a period between two stimuli) resulted in improvement of $\sqrt{800}$ in the signal-noise relation (amplitude) from spontaneously EEG. Also, a better quality of the SEP was obtained by using the algorithm for automatic artifact rejection described in previous work²³.

Spectral analysis – Denoting the SEP as the temporal sequence of *L* data samples {*s*(*n*), *n*=0,1,2,...,*L*-1}, its power spectral was obtained by²⁴:

$$P_s(f_m) = \frac{T}{L} |S[m]|^2 = \frac{T}{L} \left| \sum_{n=0}^{L-1} s(n)e^{-j2\pi m n / L} \right|^2$$

where *T*=1/*f*_s, *f*_{*m*}=*m*/*L**T*, *m*=0,1,...,*L*-1 and *S*[*m*] is the *m* coefficient of discrete-time Fourier Transform - calculated by Fast Fourier Transform algorithm (FFT) - that corresponds to *f*_{*m*} frequency. Thus, *P*_{*s*}(*f*_{*m*}) is the energy contribution of the *f*_{*m*} frequency for SEP morphology.

Stimulation artifact – The electrical stimulation of the tibial nerve produces a transient signal of high amplitude

Table 1. Short latency SEP components at Cz'-Fpz' derivation of the 21 volunteers (identified by an experienced clinician). P and N represents the valley and peak latencies corresponding to P37 and N45 components, respectively.

	Mean	Standard deviation	Maximum	Minimum
Age (years)	26.4	±5.2	42	18
Height (m)	1.72	±0.08	1.86	1.55
<i>Intensity of motor threshold (MT)</i>				
Current (mA)	13.5	±4.5	24	5
<i>First stimulation session (MT₁)</i>				
P (ms)	37.9	±2.8	44.3	32.9
N (ms)	46.8	±3.0	53.2	42
<i>Repetition session (MT₂)</i>				
P (ms)	38.1	±2.7	44.3	34.3
N (ms)	46.9	±2.5	52.7	42

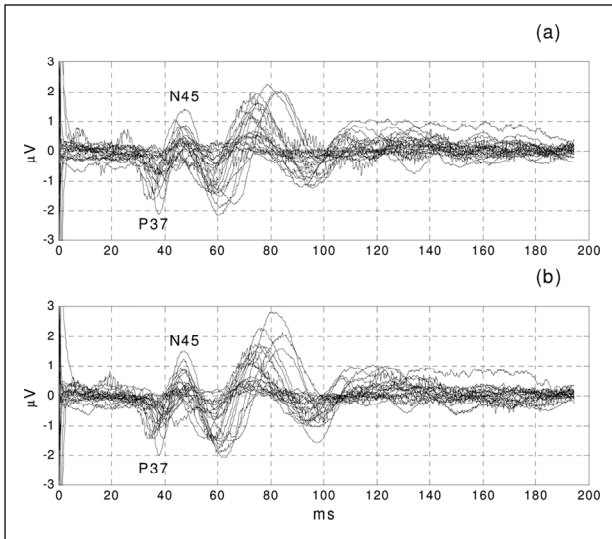


Fig 1. SEP (Cz'-Fpz' derivation) of 21 volunteers with $M=800$ epochs during (a) MT_1 and (b) MT_2 stimulation sessions.

and short time duration (stimulus artifact) synchronous and immediately after the stimulus. Thus, the effect of this artifact in the SEP was estimated by using a time-frequency analysis.

RESULTS

The SEP of the Cz'-Fpz' derivation (Fig 1) shows, as expected, the principal morphological characteristics P37 and N45^{21,22}. The data in the Table 1 evidence the similarity of the SEP's, during MT_1 and MT_2 stimulation sessions.

The time-frequency analysis of the SEP (Fig 2) indicated that the stimulus artifact contributes with high energy in the whole frequency band (0–2 kHz) up to 2 ms after the stimulus (Figs 2B and 2C). Then, the energy of the stimulus artifact decreases approximately up to 1 kHz and latency of 5 ms. The statistical comparison (non-parametric Wilcoxon test for paired data) between SEP and spontaneously EEG average (EEGa) spectrograms of the 21 volunteers also indicated a difference ($p<0.05$) up to 5 ms after the stimulus. Furthermore, notice the increment of the power contribution (approximately up to 1 kHz) in the latencies P37 and N45 in comparison with the EEGa (Fig 2B).

The power spectrum of a rectangular window (5–195 ms) of a SEP during MT_1 (Fig 3) shows the energy concentrated up to 100 Hz (99%). On the other hand, the EEGa spectrum shows relative contributions of power in higher frequencies, approximately up to 1 kHz (99%). Similar observations were carried out for all the volunteers and during MT_2 .

The frequencies corresponding to the maximum

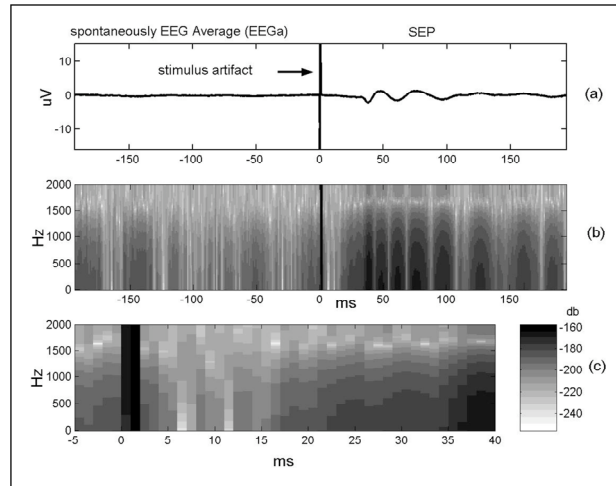


Fig 2. (a) Spontaneously EEG average (EEGa, -194 to 0 ms) and SEP during MT_1 (0 to 194 ms), for the volunteer #21 and $M=800$ epochs. (b) Spectrogram using a 1 ms Hann window, without overlapping but with zero padding, resulting in a spectral resolution of 10 Hz. (c) zoom of (b).

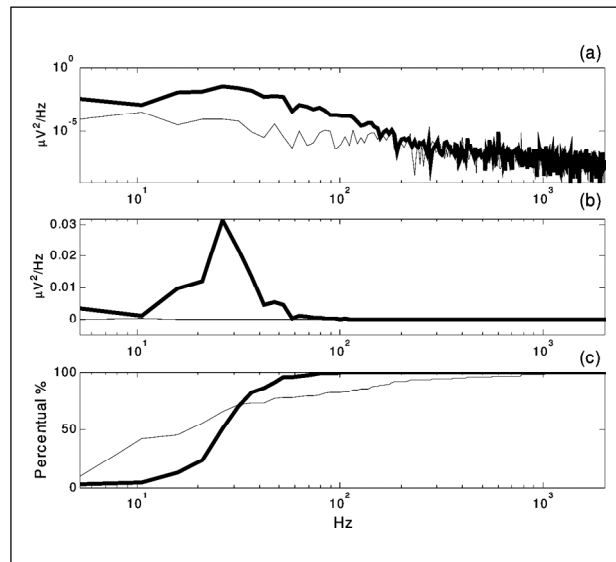


Fig 3. Power spectra of the SEP ($M=800$ epochs) during MT_1 (thick line) and the EEGa ($M=800$ epochs) just before the stimulation (thin line) of the volunteer #21. The power spectra were obtained using a rectangular window of 190 ms duration (spectral resolution of 5.3 Hz), from 5 to 195 ms latencies for the SEP. (a) logarithmic scale, (b) linear scale, and (c) percent of the relative accumulated energy.

peak of the SEP spectrum, during MT_1 stimulation, in the 21 volunteers (Table 2) indicate that the band from 5 to 58 Hz, with median equal to 21 Hz (Table 3), contributes with the most power for the SEP morphology. On the other hand, the EEGa spectrum contains the maximum peaks in the 5–780 Hz band, with median equal to 10 Hz. The Wilcoxon test (Table 3)

Table 2. Frequency corresponding to the maximum peak of the SEP spectrum during MT₁ stimulation in the 21 volunteers (in parentheses values for EEGa spectrum).

Frequency (Hz)					
#1	10.6 (21.1)	#8	10.6 (10.6)	#15	15.8 (10.6)
#2	15.8 (780.6)	#9	31.7 (10.6)	#16	58.0 (10.6)
#3	31.7 (26.4)	#10	31.7 (10.6)	#17	36.9 (10.6)
#4	5.3 (10.6)	#11	5.3 (5.3)	#18	15.8 (10.6)
#5	31.7 (5.3)	#12	15.8 (10.6)	#19	21.1 (10.6)
#6	15.8 (5.3)	#13	15.8 (31.6)	#20	26.4 (10.6)
#7	31.7 (10.6)	#14	31.7 (21.1)	#21	26.4 (10.6)

Table 3. Statistics for frequency corresponding to the maximum peak of the SEP spectrum (in parentheses values for EEGa spectrum just before stimulation)

	MT ₁	MT ₂
Median (Hz)	21.1 (10.6)	15.8 (10.6)
Minimum (Hz)	5.3 (5.3)	10.6 (5.3)
Maximum (Hz)	58.0 (780.6)	31.7 (780.6)
p (Wilcoxon)	0.03	0.19

was applied to these frequency bands and it indicated a significant difference between SEP and EEGa for MT₁ (p=0.03), although it was not the case for MT₂ (p=0.19). Thus, alternatively, the Wilcoxon test was applied to each frequency component of the SEP and EEGa spectra in the 21 volunteers. A significant difference (p<0.01) was found in low frequencies, approximately up to 100 Hz (Fig 4), being the range from 30 to 58 Hz the band with most significance difference (p<0.0001). This result was similar for MT₂ stimulation session.

DISCUSSION

The time-frequency analysis of the tibial SEP indicated a significant effect (p<0.05) of the stimulus artifact in the frequency components of the SEP approximately up to 5ms after the stimulus. In previous studies, the presence of this artifact in the tibial SEP was considered up to 3 ms²⁵, 5 ms²⁶, and 10 ms²⁷. Erwin et al.²⁸ reported that this artifact can be avoided by beginning the analysis from 1 to 5 ms after the stimulus, which depend on the stimulated nerve. Therefore, it is not still established the initial instant for analysis of the tibial SEP. Thus, the use of the time-frequency analysis, together with the statistical infer-

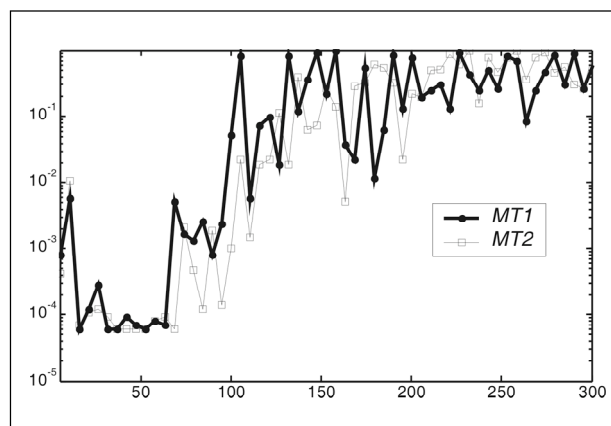


Fig 4. p-value of statistical comparison (Wilcoxon test for paired data) between each frequency component of the SEP spectrum and EEGa spectrum just before stimulation. MT₁ (thick line) and MT₂ (thin line) sessions.

ence, it can contribute to determine the stimulation artifact duration, although this procedure cannot guarantee the identification of the long and slow components of this artifact, because they can be overlapped on the physiologic response.

The frequency of the maximum power of the SEP spectrum, for the group of 21 volunteers, indicated the band up to 58 Hz as the best to identify the evoked response to the posterior tibial stimulation. Although this procedure is similar to the adopted by Basar et al.¹⁴, this band was not statistically different (p=0.19) to the EEGa band (up to 780 Hz) during MT₂ stimulation session. Such evidence suggests that the spectral analysis alone is not the most appropriate procedure to differentiate bands between the SEP and EEGa. The Wilcoxon test applied to each frequency component of the SEP and EEGa spectra shows significant difference (p<0.01) up to 100 Hz for both MT₁ and MT₂ stimulation sessions. This finding suggests that there is relevant information in other frequency bands than the 13-55 Hz range used by Gobelé et al.¹⁰ in their study of the relation between the sensory process (tibial and median nerves) and the attention. However, it is worth to point out that the frequency components with higher contribution to the SEP morphology are within the range from 30 to 58 Hz (significance level, p<0.0001). Nakano and Hashimoto¹⁹ have also found that the energy of the tibial SEP spectrum is concentrated in the range 40–60 Hz, although distributed from 20 to 300 Hz. By stimulating other nerves, Noss et al.²⁹ reported the low frequencies (up to 100 Hz) as those with higher contribution to the somatosensory response in the human being.

Tibial somatosensory evoked potential is now being broadly introduced into clinical practice and intraoperative monitoring^{30,31}. With this aim, normal values of SEP parameters are essential for a reliable application. The effect of subject height, age and gender on latency, inter-peak interval and amplitude characteristics of tibial SEP was recently investigated³¹. In this kind of studies, the time-frequency analysis here applied, as well as the frequency components that better characterize the SEP is fundamental for investigating the brain oscillations due somatosensory stimulation. Moreover, these frequencies could be considered for somatosensory evoked potential intraoperative monitoring and clinical applications.

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