"Exploration of nociceptive cortical processing with steady-state evoked potentials"

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Abstract

The periodic presentation of a sensory stimulus induces, at certain frequencies of stimulation, a sustained electroencephalographic response known as steadystate evoked potentials (SS-EP). SS-EPs are considered to reflect entrainment of cortical sensory networks resonating at the frequency of stimulation. In the present study we characterize and compare SS-EPs elicited by the selective electrical activation of nociceptive Aδ-fibers and non-nociceptive Aβ-fibers. Nine subjects took part in the experiment. Ten second trains of nociceptive (intra-epidermal electrical stimulation) and non-nociceptive (transcutaneous electrical stimulation) stimuli were applied to the left and right hand in separate blocks. Trains consisted of 0.5 ms constant-current pulses modulated at 3, 7, 13, 23 and 43 Hz. Consistent nociceptive and non-nociceptive SS-EPs were recorded at all stimulation frequencies. Whereas non-nociceptive SS-EPs were maximal over the parietal region contralateral to the stimulate...

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Exploration of nociceptive cortical processing with steady-state evoked potentials

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Introduction

Studies have shown that the periodic repetition of a stimulus induces, at certain stimulation frequencies, a sustained electro-cortical response of corresponding frequency, referred to as steady-state evoked potentials (SSEPs)¹. Using infrared laser stimulation, we recently showed that SSEPs can be used to explore nociceptive cortical processing². Here, we implemented a novel approach to elicit such responses, using a periodic intra-epidermal electrical stimulation of cutaneous A δ -nociceptors (A δ -SSEPs). Using a wide range of frequencies (3, 7, 13, 23 vs. 43 Hz), we compared the scalp topographies and the temporal dynamics of these A δ -SSEPs to the $A\beta$ -SSEPs elicited by non-nociceptive transcutaneous electrical stimulation, as well as to the transient event-related potentials (A δ - and A β -ERPs) elicited by the onset of the 10-s stimulation trains, which were applied to the left and right hand.

Methods

- EEG: 64 scalp electrodes, 1,000 Hz sampling-rate
- 9 participants
- Two types of stimulation: A δ stimulus vs. A β stimulus

- Aδ stimulus: nociceptive intra-epidermal electrical stimulation of the hand dorsum (sensory territory of the superficial radial nerve) 3,4 .

- Aβ stimulus: non-nociceptive transcutaneous electrical stimulation of the superficial radial nerve at the level of the wrist.

- Stimulus intensity : $A\delta$ stimulus: 0.24 ±0.03 mA A β stimulus: 1.13 ±0.41 mA $(2x detection threshold to a single 0.5 ms pulse)^4$

- Two sites of stimulation: right hand vs. left hand.
- Five stimulation frequencies: 3, 7, 13, 23 and 43 Hz.
- Five stimulation blocks Each block consisted in 10 trains of electrical pulses lasting 10 s, modulated at the corresponding stimulation frequency, and separated by a 10 s ITI.
- After each stimulation train Subjects were asked to report the intensity of perception using a numerical rating scale (NRS: 0-10).

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Consistent SSEPs were obtained for all stimulus types, stimulus locations and stimulation frequencies. After subtraction of the surrounding frequency bins to account for residual background noise, the magnitude of both nonnociceptive A β -SSEPs and nociceptive A δ -SSEPs, averaged across all scalp channels was signicantly greater than zero (all t >2.42, p <0.04).



Effect of stimulation frequency



A. The magnitude of both A β - and A δ -SSEPs was dependent on the frequency of stimulation, being greater at low and high frequencies of stimulation. **B.** For non-nociceptive A β stimulation, low-frequency stimulation was perceived as more intense than high-frequency stimulation. In contrast, frequency of stimulation had little or no effect on the intensity of perception elicited by A δ -stimulation.

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A. For all stimulation frequencies, the magnitude of A δ -SSEPs remained constant throughout the 10-s train. The magnitude of A β -SSEPs remained also constant, except when stimulating at 3 Hz. B. The magnitude of both A δ and A β -SSEPs was largely unaffected by stimulus repetition across blocks.

Conclusion

Our result show that consistent nociceptive SSEPs can be obtained by the selective, rapid and periodic intraepidermal electrical stimulation of nociceptive free nerve endings, using a wide range of frequencies (3-43 Hz). At 3 Hz, the topographies of A β - and A δ -SSEPs were both maximal at the vertex, and resembled that of the late P2 wave of transient ERPs, suggesting activity originating from the same neuronal populations. The magnitude of 3 Hz A β -SSEPs also show marked habituation, suggesting that these responses were mainly related to unspecific, attention-related processes. In contrast, **at frequencies >3 Hz**, the topographies of A β - and A δ -SSEPs were markedly different. A β -SSEPs were maximal over the contralateral parietal region, while Aδ-SSEPs were maximal over midline frontal regions, thus indicating an entrainement of distinct neuronal populations. Furthermore, the responses showed no habituation, suggesting more obligatory and specific stages of sensory processing.





The onset of both the A β and A δ stimulation trains elicited a clear ERP consisting of a late negative and positive wave, whose scalp topographies were maximal at the scalp vertex. For all stimulation frequencies > 3 Hz, no later ERPs could be identified within the 10-s average waveforms. In contrast, when **non-nociceptive Aß stimuli were** applied at 3 Hz, the average waveforms appeared to be composed of a succession of ERPs, whose magnitude decayed rapidly as a function of time.

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