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BRAIN RESEARCH

Research Report

Pain assessment by continuous EEG: Association between subjective perception of tonic pain and peak frequency of alpha oscillations during stimulation and at rest

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ARTICLE INFO

Article history:
Accepted 3 May 2010
Available online 9 May 2010

Keywords:
Tonic pain
Psychophysics
Electroencephalography (EEG)
Alpha oscillations
Peak frequency

ABSTRACT

Recordings of neurophysiological brain responses to noxious stimuli have been traditionally based on short stimuli, in the order of milliseconds, which induce distinct event-related potentials (ERPs). However, using such stimuli in the experimental setting is disadvantageous as they are too brief to faithfully simulate clinical pain. We aimed at utilizing continuous EEG to investigate the properties of peak alpha frequency (PAF) as an objective cortical measure associated with subjective perception of tonic pain. Five minute long continuous EEG was recorded in 18 healthy volunteers under: (i) resting-state; (ii) innocuous temperature; and (iii) psychophysically-anchored noxious temperature. Numerical pain scores (NPSs) collected during the application of tonic noxious stimuli were tested for correlation with peak frequencies of alpha power-curves derived from central, temporal and frontal electrodes. NPSs and PAFs remained stable throughout the recording conditions (RM-ANOVAs; $Ps > 0.51$). In the noxious condition, PAFs obtained at the bilateral temporal scalp were correlated with NPSs ($Ps < 0.001$). Moreover, resting-state PAFs recorded at the bilateral temporal scalp were correlated with NPSs reported during the noxious condition ($Ps < 0.01$). These psychophysical-neurophysiological relations attest to the properties of PAF as a novel cortical objective measure of subjective perception of tonic pain. Moreover, resting-state PAFs might hold inherent pain modulation attributes, possibly enabling the prediction of individual responsiveness to prolonged pain. The relevance of PAF to the neural processing of tonic pain may indicate its potential to advance pain research as well as clinical pain characterization.

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doi:10.1016/j.brainres.2010.05.004

1. Introduction

Neurophysiological studies of experimental pain, which aim at revealing indirect indices of neural activity through time-locked event-related potentials (ERPs), employ phasic, brief stimuli, in the order of milliseconds, which are too short to faithfully simulate the experience of clinical pain. Experimental tonic pain, on the other hand, is a stimulus which better resembles the sensory experience in the clinical setting (Huber et al., 2006). While extensive functional imaging-based data have been gathered regarding experimental tonic noxious stimuli (Peyron et al., 2000; Ringler et al., 2003; Schreckenberger et al., 2005; Owen et al., 2010), little is known about the changes in the EEG frequency content during the processing of such stimuli. Recording and electrophysiological characterization of cortical responses to tonic pain require methods other than ERPs, namely continuous EEG.

Continuous EEG is commonly analyzed by transforming data from the time domain to the frequency domain. The transformed data is characterized by a curve of the amplitude of power–density plotted against the frequency range of interest. The area under this curve is the frequency content of the observed activity. A significant measure derived from such analysis is the highest power–density point within the investigated frequency range. This peak-point is identified by two parameters: (i) the frequency at which it occurs on the frequency axis, and (ii) its amplitude on the power–density axis.

Within the frequency domain, alpha-band oscillations (7.5–12 Hz) are the most explored frequencies. These oscillations are widely distributed in the cerebral cortex, and their peak amplitude was found to decrease in the corresponding cortical regions during somatosensory stimuli and voluntary movements (Pfurtscheller and Lopes da Silva, 1999; Fu et al., 2001; Cheyne et al., 2003; Stančák et al., 2003; Feige et al., 2005). Similar decreases in alpha amplitudes were also reported to be induced by experimental pain (Chen and Rappelsberger, 1994; Chen et al., 1998; Chang et al., 2001a,b, 2002a,b; Ploner et al., 2006; Dowman et al., 2008). While alpha oscillations may conjointly represent cognitive performance, lower and higher frequencies have been associated with attentional processes and specific task requirements, respectively (Klimesch, 1999).

The measure of peak alpha frequency (PAF) has not yet been explored in the context of tonic pain processing. In other experimental paradigms, PAF has been described repeatedly as a stable measure (Poulos et al., 2002; Maltez et al., 2004; Vuga et al., 2006), increasing with cognitive processing, attentional demands and arousal (Köpruner et al., 1984; Klimesch et al., 1990; Li et al., 1996). A large study of 688 twins found PAF to be highly heritable (Posthuma et al., 2001), and the intra-individual stability of PAF was suggested to qualify this parameter as a 'personal signature' due to its high reproducibility (Näpflin et al., 2007). Moreover, a study of 550 normal subjects aged 11–70 revealed that PAF was positively correlated with working memory performance across the lifespan (Clark et al., 2004).

These advantages of the PAF measure, which are lacking in the peak alpha amplitude, together with the novelty of associating PAF with processing of tonic pain, motivated us to focus on this measure. Specifically, the present study aimed at investigating whether PAF values induced by tonic noxious thermal stimuli could serve as an objective cortical measure associated with the subjective perception of tonic heat pain.

2. Results

2.1. Psychophysics

In the present study, subjects were stimulated on the left, non-dominant volar forearm, using a contact-heat thermode for 5 min at each of two intensities: (i) 32 °C and (ii) 'pain-60' temperature, which had been determined in a preliminary session for each individual as the temperature that induced a pain experience at a magnitude of 60 on a 0–100 numerical pain scale during a 30-second stimulus (Granot et al., 2006, 2008; Weissman-Fogel et al., 2009).

The mean 'pain-60' temperature was 45.15±1.19 °C. The mean numerical pain scores (NPSs) obtained at 100 s, 200 s, and 300 s for the tonic stimuli of the noxious condition were 60.91±15.59; 54.27±13.39; and 55.39±18.21, respectively. An insignificant one-way RM-ANOVA ($P=0.68$) indicated no significant differences between the three NPSs which were reported during the application of the tonic noxious stimulation. This affirms the steady perception of a painful sensory experience throughout the noxious condition, and justifies the averaging of the three NPSs for further analysis. The grand-average of NPSs collected during tonic stimulation application was 56.33±14.03. The average of the fourth NPS, reflecting the overall pain experience during the tonic noxious stimulation, was 56.17±10.88. A paired two-tailed *t*-test revealed no significant difference between the grand-average of the NPSs collected during the tonic noxious 'pain-60' intensity and the fourth overall NPS collected after the stimulus ending ($P=0.87$).

2.2. PAFs in the EEG recording conditions

An insignificant two-way RM-ANOVA for each recording condition indicated no significant differences between the three averaged PAFs attributed to each third of the recorded data at the examined electrodes (resting-state: $P=0.518$; innocuous condition: $P=0.641$; noxious condition: $P=0.708$). These analyses attest to the stability of the PAF measure throughout the recording conditions and justify the averaging of the PAF values of the three epochs for further analysis. A significant two-way RM-ANOVA analysis ($F_{12,340}=6.577$; $P<0.001$) pointed to a statistical interaction among the factors Condition and Recording electrode location. A statistically significant change in PAFs between conditions (resting-state, innocuous and noxious) was indicated by the post-hoc Tukey–Kramer test only at the temporal electrodes ipsilateral ($P=0.028$) and contralateral ($P=0.015$) to the applied stimulation, namely T_7 and T_8, respectively. At these electrode positions, mean PAF values increased from 9.19±0.89 and 9.49±0.98 Hz under the resting-state condition, to 9.56±0.81 and 9.93±0.87 Hz under the innocuous condition, and to 10.07±1.05 and 10.49±1.12 Hz under the noxious condition, respectively. Table 1 describes the linear associations between PAFs of the continuous EEG recorded at the C_z, C_3, C_4, T_7, T_8, F_{p1} and F_{p2} electrodes during the resting-state, innocuous, and noxious conditions (presented *P*-values are post Bonferroni corrections

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