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Heart cycle-related effects on event-related potentials, spectral power changes, and connectivity patterns in the human ECoG

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ABSTRACT

The perception of one's own heartbeat is a fundamental interoceptive process that involves cortical and subcortical structures. Yet, the precise spatiotemporal neuronal activity patterns underlying the cortical information processing have remained largely elusive. Although the high temporal and spatial resolution of electrocorticographic (ECoG) recordings is increasingly being exploited in functional neuroimaging, it has not been used to study heart cycle-related effects. Here, we addressed the capacity of ECoG to characterize neuronal signals within the cardiac cycle, as well as to disentangle them from heart cycle-related artifacts. Based on topographical distribution and latency, we identified a biphasic potential within the primary somatosensory cortex, which likely constitutes a heartbeat-evoked potential (HEP) of neuronal origin. We also found two different types of artifacts: i) oscillatory potential changes with a frequency identical to the heart pulse rate, which probably represent pulsatility artifacts and ii) sharp potentials synchronized to the R-peak, corresponding to the onset of ventricular contraction and the cardiac field artifact (CFA) in EEG. Finally, we show that heart cycle-related effects induce pronounced phase-synchrony patterns in the ECoG and that this kind of correlation patterns, which may confound ECoG connectivity studies, can be reduced by a suitable correction algorithm. The present study is, to our knowledge, the first one to show a focally localized cortical HEP that could be clearly and consistently observed over subjects, suggesting a basic role of primary sensory cortex in processing of heart-related sensory inputs. We also conclude that taking into account and reducing heart cycle-related effects may be advantageous for many ECoG studies, and are of crucial importance, particularly for ECoG-based connectivity studies. Thus, in summary, although ECoG poses new challenges, it opens up new possibilities for the investigation of heartbeat-related viscerosensory processing in the human brain.

Introduction

The investigation of heart cycle-related brain activity in the context of conscious perception of one's own heartbeat has become a prominent topic in recent years (Bechara and Naqvi, 2004; Critchley et al., 2004; Khalsa et al., 2009; Pollatos et al., 2007; Tracy et al., 2007). Heartbeat-evoked potentials (HEPs) have been frequently investigated with EEG (Dirlich et al., 1998; Fukushima et al., 2011; Gray et al., 2007; Leopold and Schandry, 2001; Montoya et al., 1993; Pérez et al., 2005; Pollatos and Schandry, 2004; Pollatos et al., 2005; Schandry and Montoya, 1996; Schandry and Weitkunat, 1990; Schandry et al., 1986; Shao et al., 2011; Yuan et al., 2007) and were found to be modulated by psychological factors such as attention, motivation and the ability to consciously perceive heartbeats. Sources of the reported HEPs that were frequently discussed include the somatosensory and frontal cortex (Dirlich et al., 1998; Leopold and Schandry, 2001; Montoya et al., 1993; Pollatos and Schandry, 2004; Schandry and Weitkunat, 1990; Schandry et al., 1986) as well as cingulate and insular regions (Cameron and Minoshima, 2002; Critchley et al., 2004; Khalsa et al., 2009; Pollatos et al., 2005). Different latencies of the HEP were reported, ranging from 200 ms to 650 ms relative to the ECG-R-peak (Tables 1 and 2). The exact time-course of the HEP, however, was difficult to determine with the EEG because of the low EEG signal-to-noise ratio (SNR) during the time segment from the R-peak of the ECG signal until the complete decay of the T wave (Dirlich et al., 1997). This low SNR results from a heart cycle-related artifact termed the cardiac field artifact (CFA) which contaminates EEG recordings. The CFA is thought to originate from the myocardial muscle and can be measured anywhere on the body surface, including the scalp, where it is prominently seen in the EEG. The

Abbreviations: CFA, cardiac field artifact; CSF, cerebrospinal fluid; ECoG, electrocorticogram; EEG, electroencephalogram; EMG, electromyogram; ESM, electrical stimulation mapping; FDR, false discovery rate; HEP, heartbeat-evoked potential; PSI, phase synchrony index; SNR, signal-to-noise-ratio.

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Table 1
Types of heart cycle-related effects in the EEG.

	Heartbeat-evoked potential (HEP)	Cardiac field artifact (CFA)	Pulsatility artifacts due to pulsating blood vessels
Timing	Potential changes in the time interval 200 ms to 650 ms relative to the R-peak of the ECG signal. Exact time course unclear.	Sharp peak at the R-peak. Time course resembles the time course of the ECG during the QRST-complex	Peaks ~200 ms relative to the R-peak of the ECG signal. Smooth-wave- or saw-tooth-like time course with the same frequency as the pulse rate.
Spatial distribution	Regional occurrence in frontal, central and parietal EEG channels	Global occurrence in all/most EEG channels	Local occurrence in EEG channels near blood vessels

Timing and spatial distribution in the EEG as described in previous studies.

typical feature of the CFA in EEG recordings is a sharp potential peaking at the time point of the ECG R-peak (Schandry et al., 1986).

A third kind of heart cycle-related effects is pulsatility artifacts. These include artifacts originating from pulsating blood vessels, from pulsatile circulation of the cerebrospinal fluid (CSF) and from the resulting pulsatile motion of brain tissue. In EEG recordings, for example, the placing of electrodes on or near an artery is usually avoided, because pulsatility artifacts can be caused by the contraction and expansion of the blood vessel. Pulsatility artifacts in the EEG can appear with pulse-synchronous smooth wave- (Binnie, 2003; Dworetzky et al., 2010; Hirsch and Brenner, 2010; Stern, 2004) or saw-tooth-like (Cooper et al., 2003b; Zumsteg et al., 2004) time course. Corresponding artifact peaks were reported to appear invariably at ~200 ms after the ECG R-peak (Hirsch and Brenner, 2010; Zumsteg et al., 2004). In ECoG recordings, such pulse-related movement of electrode contacts due to nearby pulsating blood vessels may contribute artifact components to the recorded signals, especially in low frequencies, as suggested by Bleichner et al. (2011). Regarding the origin of pulsatile circulation of CSF, it was proposed that the change of internal pressure in the arteries during the systolic phase of the heart cycle results in an expansion of the vessel diameter which propagates into the CSF. The resulting intracranial pressure wave starts in the frontal lobe and moves into the more posterior parts of the brain, thus causing a motion of brain tissue (Enzmann and Pelc, 1992; Greitz et al., 1992; Wagshul et al., 2011). It has been proposed that this intracranial pressure wave and the resulting pulsatile motion of CSF and brain tissue may also have an impact on scalp EEG signals (Dirlich et al., 1998; Schroth and Klose, 1992a,b) and might be a source of ECoG pulsatility artifacts, as well. Characteristics of these three types of heart cycle-related effects (HEPs, CFA, and pulsatility artifacts) in EEG recordings are summarized in Table 1.

To our knowledge, systematic investigations of heart cycle-related effects in the ECoG, irrespective of whether they present bio-electrical artifacts or heart cycle-related brain activity, are lacking. ECoG recordings obtained from electrodes placed directly on the surface of the brain have advantages over non-invasive EEG recordings, including higher spatial and temporal accuracy (Engel et al., 2005), decreased susceptibility to artifact contamination and, hence, better overall signal quality (Ball et al., 2009a). Until recently, it was often assumed that major artifacts are absent in ECoG, although no quantitative investigations on the signal properties and limitations of ECoG recordings were available. In recent years, however, ocular artifacts, including eye-blink artifacts (Ball et al., 2009a) and saccade-related ocular EMG (Kovach et al., 2011) as well as chewing artifacts (Shimoda et al., 2012) were investigated in the ECoG. The proximity of blood vessels to the implanted electrode contacts was identified to be one of the most important causes of anomalous signals (Miller et al., 2009) and presumed to be the cause of the main artifact (i.e., the pulse related artifact) in ECoG recordings (Panagiotides et al., 2011). Pulsatility artifacts due to pulsating brain tissue could also contaminate ECoG recordings, given that brain pulsations are clearly visible with each heartbeat when the brain is exposed (Handy, 2004). It is, however, still unknown to what degree the different heart cycle-related effects known from EEG are present in ECoG recordings. For example, it remains unclear whether the skull insulates sufficiently to shield the brain (and ECoG recordings) from CFA contamination, and whether blood vessels can act as low conductance pathways through which the CFA may "tunnel" into the intracranial cavity.

Clarification of the role of heart cycle-related effects in the ECoG is important for several reasons. For example, to study heart cycle-related neuronal processing with ECoG, it is necessary to reliably distinguish neuronal signal components from others in the ECoG. As another example, variability induced by heart cycle-related effects in ECoG could lead to alterations of functional connectivity maps, comparable to the consequences of pulsatility artifacts in functional magnetic resonance imaging (fMRI), where it was argued that changes in pulse rate can significantly alter the results of functional connectivity analyses (Chang et al., 2009). Similarly, in the ECoG, pulsatility-artifact-evoked phase synchrony or changes in other connectivity measures could be misinterpreted as indexing neural functional connectivity.

The aim of the present study was to characterize heart cycle-related effects in ECoG recordings. Based on the EEG literature, we expected (i) HEPs in the time range from 200 ms to 650 ms relative to the ECG R-peak, located over the somatosensory and/or frontal cortex and/or cingulate/insular regions; (ii) the CFA, most prominently during the QRS complex and to a lesser extent during the T wave; and (iii) pulsatility artifacts with a smooth wave- or saw-tooth-like time course, with the same frequency as the pulse rate and with higher amplitudes than in the EEG, due to the greater proximity of the ECoG electrodes especially to blood vessels. In addition to potentials in the time domain, we were also interested in effects in the time–frequency domain because heart cycle-related spectral power modulations of ECoG activity had, to our knowledge, not yet been analyzed with electrophysiological recordings. Yet, at the same time, many previous ECoG studies rely on time–frequency representations of ECoG activity (Ball et al., 2008; Crone et al., 1998a,b, 2006; Lachaux et al., 2005; Pistohl et al., 2012; Schalk et al., 2008; Sinai et al., 2005). Finally, we evaluated a template correction approach to avoid heart cycle-related phase-synchrony patterns in the ECoG.

Materials and methods

Patients and data collection

Data sets from five patients undergoing evaluation for epilepsy surgery were used for the analysis of heart pulse-related ECoG changes. Sex, age and diagnosed anatomical pathologies of these patients were: Patient 1 (P1): female, 17 years, focal cortical dysplasia in the left fronto-polar cortex; patient 2 (P2): male, 17 years, focal cortical dysplasia in the left prefrontal cortex; patient 3 (P3): female, 16 years, focal cortical dysplasia in the right premotor–prefrontal cortex; patient 4 (P4) male, 47 years, focal cortical dysplasia right occipital-lateral cortex; patient 5 (P5) female, 26 years, dysplasia in the left temporal lobe; and patient 6 (P6) male, 19 years, dysplasia in the left prefrontal cortex. Written informed consent was obtained from all patients, stating that the electrophysiological data obtained during the diagnostic process might be used for scientific purposes.

The ECoG was recorded with subdurally-implanted grid- and strip-electrodes using a clinical AC EEG-System (IT-Med, Germany) with sampling rates of 256 Hz (P1, P2 and P3) and 1024 Hz (P4). Recordings were hardware high-pass filtered with a 0.032-Hz cutoff