Clinical Neurophysiology 127 (2016) 277–284

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Comparison of subdural and subgaleal recordings of cortical high-gamma activity in humans

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ARTICLE INFO

Article history:
Accepted 26 March 2015
Available online 9 April 2015

Keywords:
High-gamma brain machine interface
Brain computer interface
Electrocorticography
Electroencephalography
Subgaleal

HIGHLIGHTS

- We compare high-gamma (70–110 Hz) brain signals recorded with subdural and subgaleal electrodes.
- Signal attenuation is modeled with linear and 1-pole filter transfer functions.
- Findings suggest that the skull does not distort or selectively filter signals.

ABSTRACT

Objective: The purpose of this study is to determine the relationship between cortical electrophysiological (CE) signals recorded from the surface of the brain (subdural electrocorticography, or ECoG) and signals recorded extracranially from the subgaleal (SG) space.
Methods: We simultaneously recorded several hours of continuous ECoG and SG signals from 3 human pediatric subjects, and compared power spectra of signals between a differential SG montage and several differential ECoG montages to determine the nature of the transfer function between them.
Results: We demonstrate the presence of CE signals in the SG montage in the high-gamma range (HG, 70–110 Hz), and the transfer function between 70 and 110 Hz is best characterized as a linear function of frequency. We also test an alternative transfer function, i.e. a single pole filter, to test the hypothesis of frequency dependent attenuation in that range, but find this model to be inferior to the linear model.
Conclusions: Our findings indicate that SG electrodes are capable of recording HG signals without frequency distortion compared with ECoG electrodes.
Significance: HG signals could be recorded minimally invasively from outside the skull, which could be important for clinical care or brain–computer interface applications.

Abbreviations: CE, cortical electrophysiological; BMI, brain machine interface; ECoG, electrocorticography; EEG, electroencephalography; HF, high frequency; HG, high-gamma; SG, subgaleal.

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http://dx.doi.org/10.1016/j.clinph.2015.03.014
1388-2457/

1. Introduction

Cortical electrophysiological (CE) signals are measures of local brain activity that are important for brain–machine interfaces (Leuthardt et al., 2004) and numerous clinical and research applications such as the diagnosis and monitoring of neurological diseases, and building on our ever-increasing understanding of systems neuroscience (Wander and Rao, 2014). Low frequency bands up to approximately 50 Hz, which include canonical bands (alpha, beta, theta) are important in clinical electroencephalographic (EEG) monitoring, and are commonly recorded with scalp-surface EEG in clinical settings (Teplan, 2002). In addition to the well established utility of low frequency CE bands, high-frequency (HF) signals in the high-gamma (HG) range are becoming increasingly important in our understanding of systems neurophysiology (Wander and Rao, 2014), clinical applications such as seizure detection and localization (Fisher et al., 1992; Worrell et al., 2004) and in brain–machine interface (BMI) applications (Leuthardt et al., 2004, 2006; Miller et al., 2011; Wander et al., 2013), and seizure detection and localization (Zelmann et al., 2014). Compared to low frequency oscillations, HG signals in the range of 70–110 Hz are held to represent focal areas of neuronal activity that are spatially localized with high temporal resolution (Crone et al., 1998; Miller et al., 2007, 2014). However, activity in the HF range is low amplitude and is difficult to resolve with non-invasive methods (Darvas et al., 2010), but comparatively easy to record with invasive methods such as intracranial electrocorticography (ECoG) (Crone et al., 1998; Freeman et al., 2000). ECoG is commonly used for long-term monitoring (days to weeks) for seizure localization in with medically intractable epilepsy, and ECoG generally yields the highest quality signals of the long term recording methods commonly used in humans. Although intra-cortical (electrodes that penetrate the cortex) recording methods exist and yield very high quality single unit activity or local field potentials (LFPs), we will exclude these methods from this discussion.

A main goal of CE recording is to obtain the highest fidelity signals with the least degree of invasiveness. Electrocorticography (ECoG) is capable of providing excellent signal-to-noise-ratio (SNR) for CE signals over 100 Hz (Crone et al., 1998) and is much less susceptible to external artifacts than EEG (Ball et al., 2009). However, ECoG requires invasive surgery to place the electrodes inside the skull on the surface of the brain, and there are potential risks such as central nervous system (CNS) infection. On the other hand, the most common non-invasive method, EEG, is typically used for recording lower frequency signals (<50 Hz), although gamma (~50–70 Hz) and HG are also present in the signal at low amplitude (Darvas et al., 2010). However, placing surface electrodes is time consuming, must be repeated for each recording session and it requires skill and patience to obtain high quality electrode contact with low impedance, which are all barriers to clinical translation of BMI applications. Further, surface electrodes are much more susceptible to external (non-cortical) electrical noise from other sources such as muscles, heartbeat, and physical movement of the leads.

An alternative to existing intracranial or skin-surface recording methods is to record CE signals in the intermediate space between the skin surface and the skull, which could improve the signal quality and long-term ease of use over traditional scalp EEG with less invasiveness than ECoG. Prior modeling studies suggest that subdermal electrodes could provide accurate measurements CE signals (Subramaniyam et al., 2011). Clinical studies have been done to record low frequency oscillations with subdermally placed electrodes (Young et al., 2006; Martz et al., 2009), and Pfurtscheller and Cooper in 1975 showed frequency-dependent attenuation up to 30 Hz in humans. However, the signal properties of subdermal recording methods are still poorly understood, particularly the spectral transfer function of the HG signal as it passes through the skull. In an attempt to understand the attenuation of higher frequencies, some researchers have done *in vitro* measurements. Oostendorp et al. (2000) showed relative frequency independent impedance from 100 Hz to 10 kHz with some decrease in impedance from 1 to 100 Hz. A study by Akhtari et al. (2002) showed very little phase change across frequencies in the impedance measurements of live skull, suggesting a lack of filtering by this tissue. Together, these studies provide some understanding of the electrical properties of the skull, however the *in vitro* nature leaves an incomplete understanding of the actual transfer function from the continuous brain activity to detector space on the skull, especially in the HG frequency range. For instance, additional factors such as the nature of these sources (e.g. amount of synchronization among a population of neurons as well as size of active cortex) and geometry of the human head could also play a major role in shaping ground-truth transfer functions.

In this study we seek to quantify the *in vivo* measurement sensitivity to the continuous human CE signal over a prolonged period as recorded by electrodes in the extracranial subgaleal (SG) space (beneath the skin and galea scalp layers, just superficial to the skull) as compared with intracranial ECoG electrodes in human patients undergoing invasive seizure monitoring (Fig. 1). By simultaneously recording SG and ECoG CE signals, we can explore the nature of the transfer function between live cortex and skull, specifically the absence or presence of filtering properties and the range of attenuation between these two types of recordings, by recording the simultaneous SG and ECoG CE signals. In this study, we fit the SG signal to the ECoG signal in the HG range using a linear transfer function and a single pole filter transfer function, and compare the fit in the lower frequencies (outside the HG range) to assess goodness of fit.

2. Materials and methods

2.1. Subjects and neural recordings

Three subjects, ages 5, 11, and 11, were studied at Seattle Children's Hospital (SCH) while undergoing intracranial seizure localization and functional brain mapping. The study complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki), and The Seattle Children's Hospital Institutional Review Board approved the study procedures. All subjects gave informed assent to participate, and informed consent was obtained from the parent or guardian.

The ECoG and SG electrode locations were based on the clinical requirements for seizure localization (Integra, Plainsboro NJ, 8×8 or 8×6 arrays, 1 cm inter-electrode distance) (Fig. 2, individual reconstructions in 2a, 2b, and 2c). SG 1×4 strip electrodes were placed facing the skull as ground and reference for the clinical recordings, which is standard clinical practice at SCH (Fig. 3). Within the 4-electrode SG strip, the two outermost electrodes were used as ground and reference while the innermost two electrodes recorded SG neural signals (Fig. 4). In all cases the two inner electrodes were a centimeter removed from the edge of the craniotomy and the skull piece that was removed during surgery was put back in place and no major open gaps in the skull were present. SG electrodes were sewed to the peri-cranium.

Cortical reconstructions were performed using custom MATLAB code as previously described by Hermes and colleagues using the clinical preoperative MRI and postoperative CT scans to co-register the electrode locations with the cortical surface renderings (Hermes et al., 2010).