High Frequency Activity Correlates of Robust Movement in Humans

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***Abstract*—The neural circuitry underlying fast robust human motor control is not well understood. In this study we record neural activity from multiple stereotactic encephalograph (SEEG) depth electrodes in a human subject while he/she performs a center-out reaching task holding a robotic manipulandum that occasionally introduces an interfering force field. Collecting neural data from humans during motor tasks is rare, and SEEG provides an unusual opportunity to examine neural correlates of movement at a millisecond time scale in multiple brain regions. Time-frequency analysis shows that high frequency activity (50-150 Hz) increases significantly in the left precuneus and left hippocampus when the subject is compensating for a perturbation to their movement. These increases in activity occur with different durations indicating differing roles in the motor control process.**

I. Introduction

The ability of humans to make rapid and robust motor movements even in the face of great uncertainty and disturbances is extraordinary. Many studies in this area have focused on motor performance from a purely behavioral perspective [1-3]. Coupling motor experiments with neural recordings is rare [4,5].

Studies that do record neural activity use fMRI, ECoG, and MEG which are not well suited to studying the neural mechanisms underlying rapid movement. Each of these techniques exhibits at least one of the following negative characteristics: low spatial resolution, low temporal resolution, or recordings far from the neural source [6].

This study joins a patient implanted using Stereo-tactic electroencephalography (SEEG) with a motor task that investigates both the rapid and robust nature of human motor capabilities. SEEG offers millisecond temporal resolution along with thorough coverage of the brain including recording sites in shallow, intermediate, and deep structures that are inaccessible with traditional methods [7]. Implementing this study required an almost yearlong effort to coordinate the SEEG recordings with the task display system and a sophisticated robotic manipulandum [8].

The center-out task has the subject make reaching movements to targets at different instructed speeds. This allows examination of neural correlates of motor control under various conditions of movement speed. In addition, during approximately 20 % of trials, a force field was randomly applied of varying magnitude and direction (hereafter referred to as a perturbation). The subjects need to overcome the perturbation in order to successfully reach the target in the allotted time. Here we examine the data from one subject, which indicates that the precuneus and hippocampus increase activity preferentially when compensating for a perturbation.

II. Methods

A. Study Subject

The subject recruited underwent SEEG depth electrode implantation for the purpose of epileptic focus localization. After the operation, a member of the research team independent of the clinical staff approached the patient to describe the research and the task. The subject enrolled voluntarily and provided informed consent under guidelines approved by the Cleveland Clinic Institutional Review Board. There are no clinical alterations other than the administration of the behavioral task.

B. Electrical Recordings

The SEEG depth electrode (PMT Corporation, MN, USA) implantation is performed at the Cleveland Clinic using stereoscopic cerebral angiograms co-registered with three-dimensional MRI scans (Fig. 1) [7]. The preoperative MRI and angiogram are used during surgery to plan out electrode insertion trajectories to avoid vascular structures to minimize the risk of a bleed. The recordings are performed on site in the Epilepsy Monitoring Unit and sampled at 2 kHz through the Nihon Kohden 1200 A EEG diagnostic and monitoring system (Nihon Kohden America, Foothill Ranch, CA, USA). The subject has 13 electrodes implanted each with 10 contacts. The contacts are platinum based, 2 mm in length, 0.8 mm wide and spaced 1.5 mm apart. Of these, one

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contact in the left hippocampus and two contacts in the left precuneus are examined here.

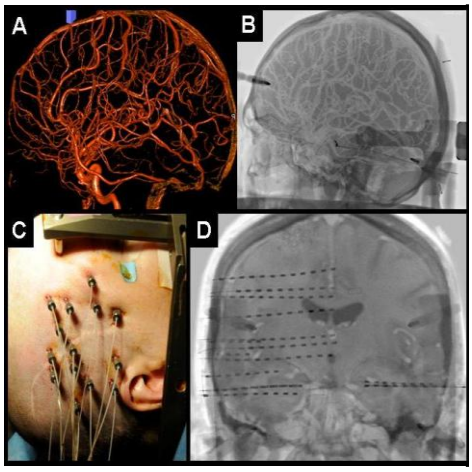

Figure 1. Imaging fusion and placement of multiple electrodes using SEEG method. (A) imaging with MRA (B) angiography (C) 14 electrodes on skin surface (D) superposition of bilateral SEEG electrodes on a coronal MRI T1weighted image.

C. Behavioral Task

The behavioral task is displayed to the subject through a computer monitor affixed to a mechanical rig with a moveable arm from the InMotion ARM Interactive Therapy System (Interactive Motion Technologies, Watertown, MA, USA), which the subject operates in order to play the game. The task is presented using Monkeylogic [9,10], an extension to Matlab (Mathworks, Natick, MA).

The task begins with a visual instruction for movement speed: slow, medium, or fast. The physical set up is illustrated in Fig. 2. Task details are laid out in Fig. 3. The exact speed range specified is based on a pre-task calibration period where the maximum speed of the subject is measured. After a 1.5 second delay, a circular target appears in the center of the screen cueing the subject to move the manipulandum-controlled cursor to the center of the screen. The cursor arriving at the home position triggers the creation of a new grey circular target in one of four possible locations: directly up, down, left, or right. After a 0.75 second delay (plus jitter), the target turns green, functioning as a go-cue.

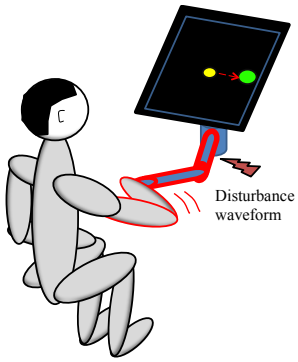

Figure 2. Subject sits in front of screen. Reaching movements are made while holding arm of robotic manipulandum. Manipulandum can record movement trajectories in addition to applying force perturbations.

Once the subject initiates movement, there is a 20% chance a perturbation will be applied. The perturbation has an equal chance of coming from any direction. Upon reaching the target, they are shown a speed feedback bar that informs them how their actual speed compares with the instructed speed. 2 seconds afterwards they are shown a reward (picture of dollar bill) or failure (picture of dollar bill with red X covering it) signal. A trial can be failed due to inability to reach and hold the target in the appropriate time frame.

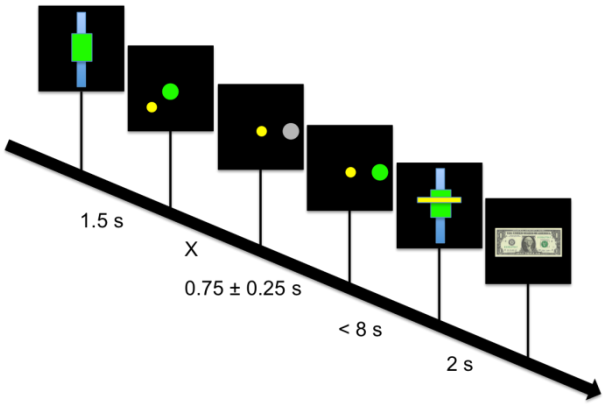

Figure 3. Slides are numbers left to right, the cursor controled by the manipulandum is yellow, and the "X" indicates the subject is given as much time as need to center the cursor. (1) bar instructing the subject how fast to move (2) home target appears (3) upon the cursor reaching the home target, a new target appears (4) the new target turns green, functioning as a go-cue (5) upon reaching the traget or failing the trial, a speed bar is shown with a horizontal yellow bar representing their actual speed (6) in the example, the movement speed is inside the allowable range, so the image of a dollar bill fucntions as a reward

D. Filtering

An 8th order Chebyshev Type I lowpass filter was applied with a cutoff frequency of 200 Hz prior to down sampling from 2000 Hz to 500 Hz. Additional band-reject filters were applied from 58-62 Hz and 118 – 122 Hz to deal with 60 Hz line noise. After the high frequency activity (HFA) metric was computed, a ½ Hz highpass filter was applied to eliminate modulations in data on time scales longer than 2 seconds.

E. Time-Frequency Analysis

The local field potential style signals collected from the SEEG electrodes do not allow direct measurement of neural spiking. Instead frequency analysis is performed on the voltage data. The spectrogram is computed using the mtspecgramc command from the Chronux toolbox in MATLAB [11]. This utilizes a multi-taper estimate scheme based on Slepian functions for calculating the power spectrum of the signal. A sliding window of 300 ms was used, incrementing by 10 ms per step. The time-bandwidth product was 2, with 3 tapers used for estimation.

F. High Frequency Analysis

Since the action potential of individual neurons cannot be extracted from the data, the high frequency activity (HFA) of the signals was examined. HFA is a metric computed from the high gamma activity (defined here at the 50-150 Hz

range) [12]. High gamma has been shown to correlate closely with neural spiking and fMRI activity [13-15]. HFA is an average of the normalized activity between 50-150 Hz.

Specifically, the log power spectrum is cut into 10 sections of 10 Hz widths (50-59 Hz, 60-69 Hz, …). The z-scored version of the log power is calculated based on the distribution of the log power in that section over the entire half hour session. The bottom 1 and top 5 percentile is excluded as a form of artifact rejection. At each time window, the z-scored log power is then averaged together across sections resulting in a single number capturing the aggregate neural firing in the volume around the electrode contact.

III. Results

A. *Perturbation versus Non-perturbation in Precuneus*

In Fig. 4 the HFA in the left precuneus is aligned to movement onset (time 0). The data from individual trials is shown, sorted based on the presence of a perturbation at the onset of movement. A clear increase in the magnitude of HFA can be seen in trails when a perturbation is applied.

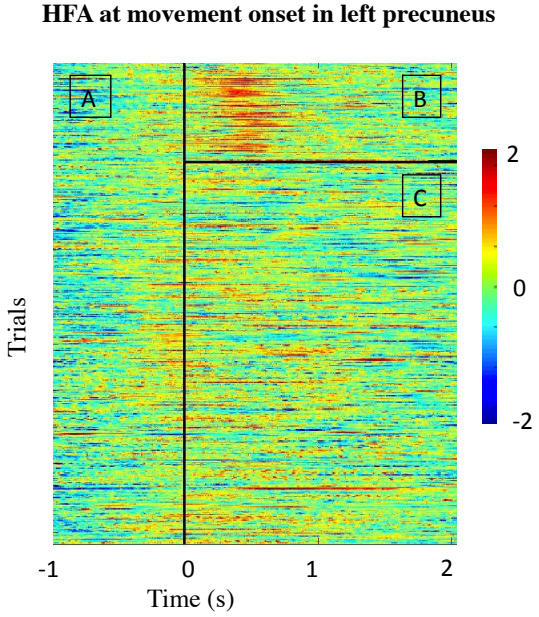

Figure 4. Normalized HFA on 2 electrode contacts in left precuneus time locked to movement onset. Each row represents the data from one trial for a particular electrode contact A) time before movement onset B) period after movement onset in trials where a perturbation was applied C) period after movement onset when no perturbatino was applied

In Fig. 5, the same data is presented differently. The HFA is time locked to the onset of movement and the average is taken across trials. The increase in the activity of the precuneus, selective to when a perturbation is applied, can be clearly seen. Notice the peak activity is seen approximately 500 ms after perturbation onset.

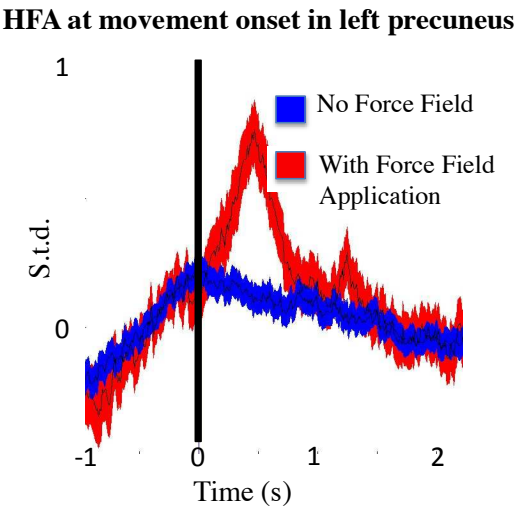

Figure 5. Average of normalized HFA on 2 electrode contacts in left precuneus time locked to movement onset. Shaded regions indicate 2 standard error of the mean, calculated across trials. The y-axis represents standard devaitions from the channel-specific mean, taken across the entire half hour session.

B. *Perturbation versus Non-perturbation in Hippocampus Tail*

In addition to the response of the left precuneus, a similar effect, although smaller in magnitude can be see in the left Hippocampus. The raw data HFA is shown in Fig. 6 where the effect is difficult to see; however, it emerges more clearly when a average is taken across all trials.

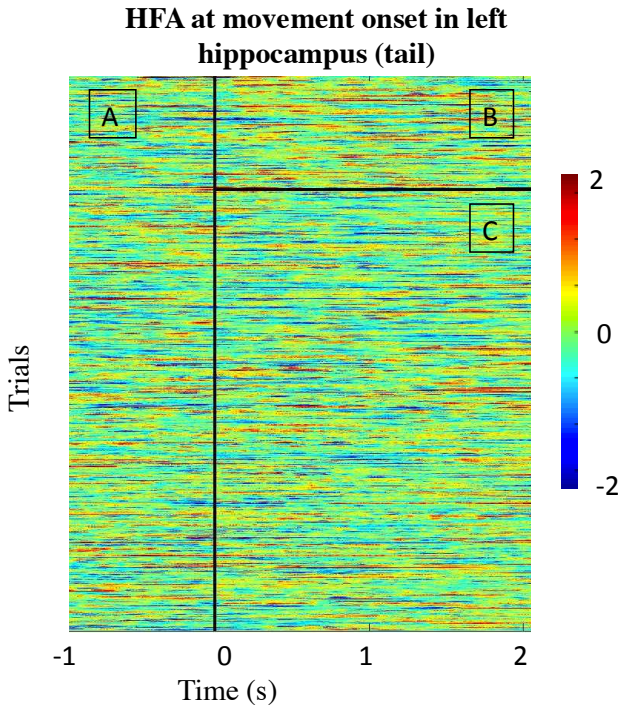

Figure 6. Normalized HFA on 3 electrode contacts in left hippocampus (tail) time locked to movement onset. Each row represents the data from one trial for a particular electrode contact A) time before movement onset B) period after movement onset in trials where a perturbation was applied C) period after movement onset when no perturbation was applied

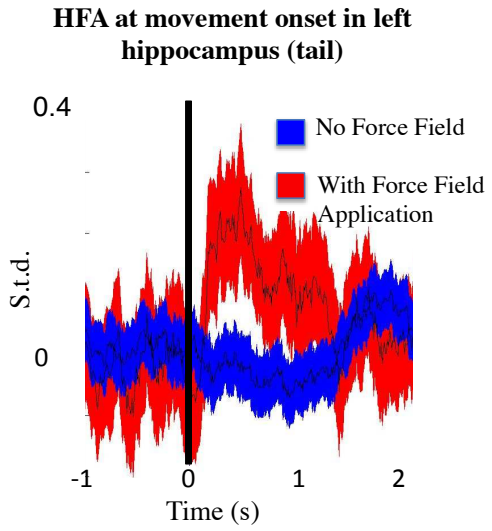

Figure 7. Average of normalized HFA on 3 electrode contacts in left hippocampus (tail) time locked to movement onset. Shaded regions indicate 2 standard error of the mean, calculated across trials.

IV. Discussion

As can be seen from the data presented here, SEEG HFA analysis has the ability to capture neural responses to cues on a trial by trial basis in regions of the brain that are very difficult to probe in human subjects. Some of the changes in neural activity shown here occur on the millisecond time scale, further supporting the use of SEEG as an incredibly useful tool in examining neural correlates.

It is not that surprising to find the precuneus responding preferentially when a perturbation is applied. The anterior region is known to be associated with the sensorimotor pathways, and it has previously been shown to monitor the success of motor behavior [16,17]. While we cannot yet pinpoint which subdivision of the precuneus our contacts are in, we may soon be able to do so by further examining the archived imaging.

The response of the hippocampus is also interesting. The hippocampus is known to play a part in spatial navigation and encoding [18]. However, we have yet to identify what exact features of the perturbation the hippocampus or precuneus is encoding. Possibilities include both perturbation magnitude and direction. We are considering direction in both absolute terms and relative to the desired movement directions.

V. Future Work

The collection of data from additional subjects and analysis of more brain regions will play a key role in allowing deeper analysis of neural responses to this task. In addition, we are a collecting the brain scans for each subject so we can reference them all to a common brain template allowing superior spatial analysis. The concurrent collection of high temporal resolution neural data from so many brain structures will allow us to perform network based analyses tracking the flow of information between brain regions.

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