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Beta-band power modulation in the human hippocampus during a reaching task

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Abstract

Objective.—Characterize the role of the beta-band (13–30 Hz) in the human hippocampus during the execution of voluntary movement.

Approach.—We recorded electrophysiological activity in human hippocampus during a reach task using stereotactic electroencephalography (SEEG). SEEG has previously been utilized to study the theta band (3–8 Hz) in conflict processing and spatial navigation, but most studies of hippocampal activity during movement have used noninvasive measures such as fMRI. We analyzed modulation in the beta band (13–30 Hz), which is known to play a prominent role throughout the motor system including the cerebral cortex and basal ganglia. We conducted the classic ‘center-out’ direct-reach experiment with nine patients undergoing surgical treatment for medically refractory epilepsy.

Main results.—In seven of the nine patients, power spectral analysis showed a statistically significant decrease in power within the beta band (13–30 Hz) during the response phase, compared to the fixation phase, of the center-out direct-reach task using the Wilcoxon signed-rank hypothesis test ($p < 0.05$).

Significance.—This finding is consistent with previous literature suggesting that the hippocampus may be involved in the execution of movement, and it is the first time that changes in beta-band power have been demonstrated in the hippocampus using human electrophysiology.

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Disclosure

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Our findings suggest that beta-band modulation in the human hippocampus may play a role in the execution of voluntary movement.

Keywords

beta-band; hippocampus; direct reach; power spectrum; modulation; stereo EEG; human; electrophysiology; center-out

1. Introduction

The hippocampus is known to play a significant role in declarative memory [1–4], spatial navigation [5–7], and learning novel motor sequences [8–10]. The medial temporal lobe is known to have white matter connections to motor regions in the frontal lobe, providing anatomic plausibility that the hippocampus may be involved in movement [11–14]. In humans, single-cell recordings have shown that neurons in the hippocampus fire during hand grasping actions [15]. The pattern of firing of these neurons mirrors those of brain areas known to be involved in motor execution, such as the supplementary motor area. Additionally, hippocampal connectivity with the sensorimotor cortex during volitional movement has been observed using functional MRI, providing additional suggestion that the hippocampus may be involved in the execution of movement [16]. However, this is still an area of ongoing research and the underlying neurophysiological mechanism of this process is not well-studied [15, 16]. The study of movement-related modulation of oscillatory activity in the human hippocampus provides the opportunity to further characterize the hippocampus' role in the execution of voluntary movement.

Most previous hippocampal research has relied on fMRI and other noninvasive measures [8, 9, 17, 18]; however, the development of stereotactic electroencephalography (SEEG) for assessing surgical candidates for epilepsy [19] has allowed for the correlation of electrophysiological neural signals with human behavior [20]. In these types of recordings, modulation of power in different frequency bands has been studied in the context of thought emergence, memories, and actions [21–23].

Specifically in the hippocampus, the theta band (3–8 Hz) is the best described of the frequency bands and has been implicated in spatial navigation and memory encoding [6, 24]. Hippocampal beta-band (13–30 Hz) changes have been studied in mice during novel object recognition [25], but the beta-band's function in the human hippocampus during movement, is not well characterized [26]. In other regions of the brain, such as the basal ganglia and motor cortex, the beta band has been studied extensively [27–30]. During rest, the beta-band is pronounced throughout the motor system including the motor cortex, pre-motor cortex, basal ganglia, cerebellum, and peripheral nervous system [27, 31]. During voluntary movement, there is a decrease in beta-band power throughout the motor system [32–34]. There is also evidence that movement inhibition is associated with an increase in beta-band power [35], a finding that has been seen in pathologic motor conditions such as Parkinson's disease [27, 28]. In non-human primates, coherent oscillations between 20–30 Hz in the motor cortex and peripheral muscles have been observed specifically during the hold phase of a gripping motor task [32]. It has also been shown that entraining cortical beta oscillations

in the human cortex leads to decreased movement speed, providing further evidence for the beta-band's role in movement execution. Additionally, after movement has been completed, a characteristic rebound in beta-band power has been observed in the motor cortex [36].

To date, it has not been clear whether these findings would also apply to the hippocampus. In this study, we utilize the classic center-out direct-reach task [37–39] to explore variations in beta-band spectral power using SEEG in the human hippocampus during a reaching task in nine patients with medically refractory epilepsy.

2. Methods

2.1. Participants

The study population consisted of nine epilepsy patients (six female) aged 20–61 years (mean 36.3 years) implanted with micro-macro depth electrodes for seizure localization and EEG monitoring. Each patient gave written, informed consent to participate in this study, and the study design was approved by the University of Southern California Health Science Campus Institutional Review Board (Study ID: HS-17-00554). The number of electrodes and their placement was personalized to each individual patient based upon video-EEG monitoring, MRI, PET scans, and seizure semiology. Each case was discussed at an interdisciplinary epilepsy conference that included neuroradiologists, epileptologists, and neurosurgeons. Seven patients had bilateral electrode placement and the remaining two had electrodes placed on only the left side. A summary of patient demographics including gender, age, handedness, and seizure-onset zone is shown in table 1. Implanted electrode information for each participant is presented in table 2.

2.2. Electrodes and recording equipment

All nine patients were implanted with micro-macro intracranial depth electrodes (MM16 A-SP05X-000, Ad-Tech Medical Instrumentation Corporation, Oak Creek, WI, USA) in the hippocampus. Each electrode had 10 micro contacts and 6 macro platinum contacts. The macro contacts were 1.57 mm in length, 1.3 mm in diameter, and spaced 5 mm apart center-to-center (figure 1). Neural signals from the macro-type electrodes were unity-gain amplified, filtered with Butterworth 1st-order analog high-pass (0.3 Hz) and 3rd-order analog low-pass (7500 Hz) filters, and digitized with 16-bit, 250-nV resolution at 30 000 samples/sec. For this study, we used a down sampled copy of these data (2000 samples/sec).

2.3. 'Center-out' direct-reach task

The movement task consists of three distinct phases (figure 2). The first phase is the Inter-Trial Interval (ITI) where there is no visual cue present on the screen (1–2 s). During the ITI phase, the participants have their right arm raised and positioned about 2 inches away from the center of the screen. The participants remained in this position while they waited for the fixation dot to appear. Next is the Fixation phase. When the fixation phase begins, the participant's right arm is already raised and positioned with their fingertips about 2 inches away from the center of the screen. At this time, a gray dot (9.53 mm radius) is displayed at the center of the screen and the participant is asked to fix their gaze on the dot (1–4 s). The participant is not touching the screen nor are they moving at this time. This

phase will be used as a baseline period without movement during the subsequent analysis. To ensure that there is no movement, the participant is monitored and recorded with a video camera at this time. Before any data analysis occurs, a researcher reviews the footage from each trial to ensure that there is no movement during the fixation phase of the trial. The last phase is the Response phase where a white target circle (15.88 mm radius) appears at one of eight locations, equidistantly spaced around the fixation dot (114.3 mm center-to-center). Target locations are shown in pseudorandom order, with 8 trials per target (64 trials total). The patient is instructed to reach to the target and double tap the screen without delay as soon as the target cue appears. The response time is defined as the time difference between the target appearance on screen and the patient's double tap. All 64 trials are performed in a single block without any interruptions between the trials. The total experiment time varied between participants given their variable response times. The mean experiment time was 362.37 s (range: 265.55 s–421.40 s). The task was programmed in MATLAB (2018b, The MathWorks, Inc. Natick, Massachusetts, USA) with the Psychophysics Toolbox Version 3 (PTB-3) and presented on a touch-screen monitor (21.5-inch LED-backlit, 1920 × 1080 pixels, 250 cd m⁻² luminance, S2240Tb, Dell Inc. Round Rock, TX, USA).

2.4. Analysis

Trials in which the patient did not double-tap the target, had a response time of less than 500 ms, or had extreme values of power (limits defined as 1.5 times the interquartile range) were excluded from analysis. A threshold of 500 ms was chosen to ensure that accidental double-taps before the threshold time were not inadvertently included in the analysis. Of the 576 trials across nine patients, only a single trial was removed for having a response time of less than 500 ms. LFP data from electrode contacts located in hippocampal gray matter were used for analysis. These contacts were identified by manually inspecting preoperative MRI scans that had been merged with postoperative CT scans. The number of electrode contacts varied for each patient because the number and placement of electrode leads were individualized to the patients' suspected seizure origin. For each patient, the number of hippocampal gray matter contacts used for analysis are presented in table 2. We conducted spectral analysis using multi-tapered spectral power computed for each trial between 0 and 200 Hz with 9 leading tapers, a time-bandwidth product of 5, and over 1024 sample points window zero-padded to 2048. The multitaper method provides superior anti-leakage properties and prevents bleeding of power to nearby frequency ranges, giving it high frequency resolution [40]. This analysis was performed with Chronux (Woods Hole, MA) [41] implemented in MATLAB® (2018b, The MathWorks, Inc. United States). Trial-averaged spectral power was computed for each phase of the trial (ITI, Fixation, and Response) trimmed by a variable amount between 0.05–0.72 s at the beginning and end of each phase to exclude the transitioning states between phases and keep the same number of samples across trials and phases. Within each trial, the size of the analysis window for each phase was trimmed to the duration of the shortest phase in the trial. For example, if the Fixation phase in a given trial was one second, then a period of one second was used for the ITI and Response phases as well. For the ITI and Fixation phases, the window was centered in the middle of the phase. For the Response phase, the window was aligned to the end of the phase (when the participant double tapped the screen).

Bootstrapped ($N = 10\,000$) confidence intervals ($\alpha = 0.05$) were constructed to visualize 95% confidence intervals of spectral power for the three phases of the trial [42]. The non-overlap of confidence intervals is not used to assess statistical significance because a significant difference can exist even with overlapping confidence intervals [43].

To assess for statistical significance, a Wilcoxon-signed rank test was conducted across each frequency bin in the beta range for each hippocampal gray matter contact in each participant. The p-value was then adjusted using false discovery rate control. The Wilcoxon signed-rank test is a non-parametric statistical hypothesis test for paired data that utilizes the magnitude of observed differences between two samples to determine statistical significance. In this study, we test the null hypothesis that $(\text{PSD}_{\text{Fix}} - \text{PSD}_{\text{Res}})$ comes from a distribution with zero median. The alternative hypothesis is that the data in $(\text{PSD}_{\text{Fix}} - \text{PSD}_{\text{Res}})$ comes from a distribution with median greater than 0 (right-tailed hypothesis test).

To investigate differences in neural modulation between different hippocampal areas (i.e. ipsilateral vs. contralateral and anterior vs. posterior), we conducted a two-tailed hypothesis test for difference in proportions. We used the Yates-corrected z-test to assess significant difference in the proportion of contacts with significant modulation between hippocampal gray matter contacts in the areas of interest. The test statistic for this test is a z-score defined by the following equation:

$$z = \frac{|\hat{p}_{\text{contra}} - \hat{p}_{\text{ipsi}}| - \frac{1}{2}\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}{\sqrt{\hat{p}(1 - \hat{p})\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}},$$

Where $\hat{p}_1$ and $\hat{p}_2$ are the proportions of significant to total number of contacts found in a specific area for samples n_1 , n_2 are the total number of contacts for their respective samples and $\hat{p}$ is the proportion of significant to total number of contacts for the combined samples.

3. Results

In seven of the nine patients, power spectral analysis showed a statistically significant decrease in power within the beta band (13–30 Hz) during the response phase, compared to the fixation phase, of the center-out direct-reach task using the Wilcoxon signed-rank hypothesis test ($p < 0.05$). Contiguous frequency bins with statistically significant power differences between the response and fixation phases after adjusting for false discovery rate are presented in table 3. This includes both the average frequency range of statistically significant trial-averaged power modulation in addition to the number of electrode contacts in hippocampal gray matter that showed statistically significant power modulation for each patient. Of note, the decrease in power was evident throughout the majority of the beta-band for two patients (P024 and P026), whereas the other five patients showed a statistically significant drop in power throughout narrower subsets of the beta band. Two patients (P030 and P033) showed no statistically significant modulation in any contiguous frequency ranges.

In order to visualize the beta-band power modulation across patients, individual power spectral densities for a representative hippocampal gray matter contact for each participant in our study are presented in figure 3. This figure includes coronal, sagittal, axial, and probe's eye views of the merged CT/MRI imaging with the representative electrode contact indicated with a red arrow. Figure 3(A) contains the power spectral densities for the six patients with non-overlapping confidence intervals between the Response and Fixation phase beta-band power. Figure 3(B) contains the power spectral densities for the three patients with overlapping confidence intervals between the Response and Fixation phase beta-band power.

Six of the seven patients with significant decreases in beta-band power during the response phase of the trial showed a statistically significant return to baseline beta-band power during the subsequent ITI phase (Wilcoxon hypothesis test, $p < 0.05$). The decrease in beta power was limited to the movement phase of the experiment. A representative participant that illustrates this observation is shown in figure 4.

In order to determine if motor-related activity is differentially represented in the anterior vs. posterior hippocampus, we separately analyzed the anterior hippocampal and posterior hippocampal gray matter electrode contacts. There was no statistically significant difference in the proportion of electrode contacts with significant modulation between these two areas (Yates-corrected z-test, $p = 0.67$). Therefore, we do not believe that the location of electrode contacts in these structures explains the lack of significant modulation seen in the two participants in this study. The full results for the anterior and posterior hippocampal gray matter contacts are presented in table 4.

In order to determine if motor-related activity is differentially represented in the ipsilateral vs. contralateral hippocampus, we separately analyzed the ipsilateral and contralateral hippocampal gray matter electrode contacts. There was no statistically significant difference in the proportion of electrode contacts with significant modulation between these two areas (Yates-corrected z-test, $p = 0.35$). The full results are presented in table 5.

4. Discussion

We observed a significant drop in beta-band power in the human hippocampus during execution of a reaching task. This finding is consistent with previous literature showing that the hippocampus may play a role in the execution of movement [15]. However, to our knowledge, this is the first report of beta-band modulation in the human hippocampus during movement. That the change is related to voluntary movement is further supported by a return to baseline during the ITI phase of the following trial.

Previous work regarding the beta band in the hippocampus has been primarily focused on reward signaling in rats [44] and novel object recognition in mice [25], but its role in the human hippocampus has not been as thoroughly studied [26]. Beta-band activity is known in neurophysiology research to decrease during volitional movement in the motor cortex [32, 33, 45], which is similar to our observations in human hippocampus. In addition, changes in beta-band power have been seen in the subthalamic nucleus during movement tasks. For

instance, in ‘nogo’ trials of movement tasks, where patients are asked to start and then subsequently stop a voluntary movement when presented with a visual ‘stop’ stimulus, there is evidence of beta-band power increase in the STN [46]. The beta band has also been associated with motor system inhibition in pathologic conditions such as Parkinson’s disease [27, 29]. This previous research has led to speculation that the beta band may be a state-change signal rather than being specific to a cognitive or motor activity [28]. Further research is warranted to determine if the movement-related beta-band power change that we observe in the hippocampus is seen in other conditions as well. Further research is also warranted to determine if the observed power modulation is specific to the beta frequency band. Although there were no theta-band power changes observed during movement in our study, changes in theta-band power have been previously described in the hippocampus [24].

Because the hippocampus is known to play significant roles in memory [1, 4], navigation [6, 7], and learning motor sequences [8, 10], this study used the center-out direct-reach task in an attempt to isolate the effect of movement execution on the hippocampus. The target locations randomly appeared in one of eight locations, and the beta-band modulation was specifically seen in the response phase of the task during which the patient was required to move an arm to tap the target. With these controls, the effect is likely related to the physical act of moving. It is less likely related to learning a motor sequence or location recall because there was no predictable pattern to where the targets appeared, and because patients were instructed to move their hand to the target as soon as the cue appeared (no delay or memory period). There was less concern for the confounding effect of spatial navigation on the results given that the patient spent the duration of the task in the same physical location. However, it is still possible the beta-band modulation may be related to other task-related confounds that we could not control for, such as eye movements.

Other limitations include that the effect was seen in seven out of the nine patients, and that the return to baseline beta-band power was seen in only four. It is also known that patients with epilepsy have hippocampal changes not seen in healthy controls [47, 48] so it is unknown if the same modulation would be seen in those non-epileptic patients. We were also not able to assess the effect of handedness on modulation given that every patient conducted the trial with their right hand. Because beta-band power has been shown to be increased during holding, an additional potential limitation of our study design is that a comparison with beta-band power during rest could result in a smaller drop of beta-band power during movement.

Although movement-related control has been primarily observed in the contralateral hemisphere [49], a 2019 review by Bundy and Leuthardt highlights emerging research indicating that ipsilateral hemispheric activations can be used to decode specific features of movement [50]. This may explain why in this study we see movement-related beta-band modulation in both the ipsilateral and contralateral hippocampi. It is possible that the hemispheres encode different features of movement. We believe that this is an important area where future research is warranted.

There are many complex interactions underlying movement, and in this study we only looked at the hippocampus during a stereotyped movement. Beta-band modulation has

been seen in other brain areas, and the interaction between different brain regions during execution of voluntary movement is an area open for further study. A weakness in this study is the inability to compare beta-band power modulation from hippocampus with beta-band modulation in other brain areas. It is possible, for example, that the modulation we observe could be functionally related to global brain function, or it could be a result of volume conduction from basal ganglia and motor cortex. However, this study was constrained by the clinical mandate of care, meaning that we recorded from patients with a variety of number and placement of electrodes. Ideally, each participant would receive implants in the same brain areas. Without this control, we cannot make a strong statement about beta-band modulation in brain areas outside of the hippocampus until we have enough samples of these different brain areas to support a statistical analysis. We believe that the finding of beta-band modulation in the hippocampus is still important and hope to expand our analysis to explore other brain areas as more data are collected. It may also be useful to further characterize this beta-band power modulation by studying it in different contexts including directional tuning and delayed-reach tasks.

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Abbreviations

ITI	Inter-trial Interval
LFP	Local Field Potential
iEEG	Intracranial Electroencephalography
SEEG	Stereotactic Electroencephalography

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Figure 1.
Specifications of depth electrode used to record neural signals.

Figure 2.

The three phases of the 'center-out' direct-reach task. During the ITI phase, the patient waits for the fixation dot to appear (1–2 s). During the fixation phase (1–4 s), the patient points to the center of the screen while also fixing their gaze on the fixation dot. During the response phase, a target appears at one of eight random locations and the patient double taps the target.

Figure 3.

(A and B) Trial-averaged power spectrum with 95% confidence intervals for a representative hippocampal gray matter contact for each of the nine trial participants. Merged CT/MRI scans show coronal, sagittal, axial, and probe's eye views with the representative electrode contact indicated with a red arrow. (A) shows the six patients with non-overlapping 95% confidence intervals in Response and Fixation phase beta-band power and (B) shows the three patients with overlapping 95% confidence intervals in Response and Fixation phase beta-band power.

Figure 4.

(A) Trial average power spectrum with 95% confidence intervals of the three different phases of the experimental task for a representative patient (P024). The rhomboid pattern highlights the non-overlapping area between the 95% confidence intervals of the fixation and response phases. (B) Single ITI-to-ITI trial spectrogram for the same patient. A beta-band power decrease and subsequent return to baseline can be appreciated during the response phase.

Table 1.

Patient profiles.

ID	Gender	Age	Handedness	Seizure-onset zone
P024	F	45	Right	Right Insula and Frontal Operculum
P025	F	40	Right	Not Localized
P026	M	37	Not Available	Not Available
P027	F	46	Right	Right Orbitofrontal
P029	F	21	Right	Not Available
P030	M	29	Right	Right Parietal Region
P032	M	62	Right	Right Orbitofrontal
P033	F	26	Right	Right hippocampus
P034	F	21	Right	Right Hippocampus

Implanted Electrode Information.

ID	Total Number of Hippocampal Gray Matter Electrode Contacts	Total Number of Implanted Electrode Leads	Hemisphere	Implanted Brain Regions
P024	16	18	Left	Orbital, Medial Front, Lateral Front, Insula, Amygdala, Anterior Hippocampus, Posterior Hippocampus, Temporal, Parietal
P025	15	12	Right	Orbital, Medial Front, Lateral Front, Insula, Amygdala, Anterior Hippocampus, Posterior Hippocampus, Temporal, Parietal
			Left	Amygdala, Anterior Hippocampus, Posterior Hippocampus, Orbital Frontal, Cingulate, Parietal
P026	8	10	Right	Amygdala, Anterior Hippocampus, Posterior Hippocampus, Orbital Frontal Vertical, Cingulate, Parietal
			Left	Amygdala, Anterior Hippocampus, Lateral Precentral, Anterior Precentral
P027	13	11	Right	Amygdala, Anterior Hippocampus
			Left	Amygdala, Anterior Hippocampus, Posterior Hippocampus, Orbital Frontal, Temporal Pole, Occipital
P029	17	8	Right	Amygdala, Anterior Hippocampus, Posterior Hippocampus, Orbital Frontal, Occipital
			Left	Amygdala, Anterior Hippocampus, Posterior Hippocampus,
P030	8	7	Right	Amygdala, Temporal, Parietal, Anterior Hippocampus, Posterior Hippocampus,
			Left	Anterior Cingulate, Supplementary Motor, Amygdala, Parietal, Anterior Hippocampus, Posterior Hippocampus, Orbital Frontal
P032	4	9	Left	Anterior Hippocampus
P033	10	9	Right	Supplementary Motor, Anterior Cingulate, Orbital Frontal, Amygdala, Superior Temporal, Inferior Temporal, Insula, Parietal
			Left	Anterior Hippocampus
P034	12	6	Right	Amygdala, Anterior Hippocampus, Posterior Hippocampus, Posterior Temporal, Orbital Frontal, Hetero Temporal, Hetero Anterior, Hetero Posterior
			Left	Anterior Hippocampus
			Right	Orbital Frontal, Amygdala, Anterior Cavernous Malformation, Anterior Hippocampus, Posterior Hippocampus

Table 3.

Hippocampal electrode contact information.

ID	Number of Electrode Contacts in Hippocampal Gray Matter with Significant Modulation^a	Number of Successful Trials (n)	Average Frequency Range of Significant Modulation (Hz)^b
P024	16	63	13.1–28.8
P025	4	54	17.5–20.5
P026	8	61	18.9–27.0
P027	2	64	22.0–23.0
P029	2	64	19.0–20.5
P030	0	64	Not Significant
P032	1	63	24.0–26.0
P033	0	64	Not Significant
P034	7	64	16.4–20.1
AVG	4.4	62.3	18.9–23.73 ^c

^aUnder the Wilcoxon signed-rank test for multiple frequency bins within the beta band controlling for false discovery rate.

^bThe frequency range is averaged across electrode contacts located in gray matter of hippocampal structures with adjusted p-values less than 0.05 after controlling the false discovery rate.

^cAverage frequency range across participants excluding P030 and P033.

Table 4.

Anterior vs. posterior hippocampal electrode contacts.

ID	Anterior vs. Posterior	Average frequency range (Hz)	Number of Electrode Contacts in Hippocampal Gray Matter with Significant Beta-Band Modulation/Total Number of Implanted Electrode Contacts in Hippocampal Gray Matter
P024	Anterior	[13.86, 28.86]	7/7
	Posterior	[14.33, 28.78]	9/9
P025	Anterior	[16.00, 19.50]	2/8
	Posterior	[19.00, 21.50]	2/7
P026	Anterior	[18.88, 27.00]	8/8
P027	Anterior	[22.00, 23.00]	2/7
	Posterior	[-,-]	0/6
P029	Anterior	[23.00, 25.00]	1/7
	Posterior	[15.00, 16.00]	1/10
P030	Anterior	[-,-]	0/4
	Posterior	[-,-]	0/4
P032	Anterior	[24.00, 26.00]	1/4
P033	Anterior	[-,-]	0/6
	Posterior	[-,-]	0/4
P034	Anterior	[18.00, 21.25]	4/9
	Posterior	[14.33, 18.67]	3/3
AVG	Anterior (9)	[17.72, 25.56]	2.8/6.7 ^a
	Posterior (7)	[15.00, 24.93]	2.1/6.1 ^b

^a Average number across the 9 patients with **anterior** contacts (n = 60, significant = 25).

^b Average number across the 7 patients with **posterior** contacts (n = 43, significant = 15).

Table 5.

Contralateral vs. ipsilateral hippocampal electrode contacts.

ID	Contra- vs Ipsi-	Number of Electrode Contacts in Hippocampal Gray Matter with Significant Beta-Band Modulation/Total Number of Implanted Electrode Contacts in Hippocampal Gray Matter
P024	Contra-	7/7
	Ipsi-	9/9
P025	Contra-	3/8
	Ipsi-	1/7
P026	Contra-	4/4
	Ipsi-	4/4
P027	Contra-	1/5
	Ipsi-	1/8
P029	Contra-	0/8
	Ipsi-	2/9
P030	Contra-	0/8
P032	Contra-	1/4
P033	Contra-	0/3
	Ipsi-	0/7
P034	Contra-	1/4
	Ipsi-	6/8
AVG	Contra- (9)	1.9/5.7^a
	Ipsi- (7)	3.3/10.3^b

^a Average number across the 9 patients with **contralateral** contacts (n = 51, significant = 17).^b Average number across the 7 patients with **ipsilateral** contacts (n = 52, significant = 23).