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ELECTROCORTICOGRAPHIC FREQUENCY ALTERATION MAPPING: A CLINICAL TECHNIQUE FOR MAPPING THE MOTOR CORTEX

OBJECTIVE: Electrocortical stimulation (ECS) has been well established for delineating the eloquent cortex. However, ECS is still coarse and inefficient in delineating regions of the functional cortex and can be hampered by after-discharges. Given these constraints, an adjunct approach to defining the motor cortex is the use of electrocorticographic signal changes associated with active regions of the cortex. The broad range of frequency oscillations are categorized into two main groups with respect to the sensorimotor cortex: low and high frequency bands. The low frequency bands tend to show a power reduction with cortical activation, whereas the high frequency bands show power increases. These power changes associated with the activated cortex could potentially provide a powerful tool in delineating areas of the motor cortex. We explore electrocorticographic signal alterations as they occur with activated regions of the motor cortex, as well as its potential in clinical brain mapping applications.

METHODS: We evaluated seven patients who underwent invasive monitoring for seizure localization. Each patient had extraoperative ECS mapping to identify the motor cortex. All patients also performed overt hand and tongue motor tasks to identify associated frequency power changes in regard to location and degree of concordance with ECS results that localized either hand or tongue motor function.

RESULTS: The low frequency bands had a high sensitivity (88.9–100%) and a lower specificity (79.0–82.6%) for identifying electrodes with either hand or tongue ECS motor responses. The high frequency bands had a lower sensitivity (72.7–88.9%) and a higher specificity (92.4–94.9%) in correlation with the same respective ECS positive electrodes.

CONCLUSION: The concordance between stimulation and spectral power changes demonstrate the possible utility of electrocorticographic frequency alteration mapping as an adjunct method to improve the efficiency and resolution of identifying the motor cortex.

KEY WORDS: Brain mapping, Electrocorticography, Motor cortex

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Creating transient lesions or inducing overt movements through the use of direct electrocortical stimulation (ECS), either extra- or intraoperatively, has been an established practice in delineating eloquent cortex (3, 5, 26). This has been critical in minimizing the risk in neurological surgeries that involve seizure focus, tumor, or vascular malformation resections (1, 4, 11). To date, this is considered the "gold standard" and has been shown in a high number of patients to be predictive of functional outcome (11, 17). ECS, however, is still coarse in its ability to delineate regions of motor and speech cortex. Effective mapping requires that all electrodes be individually stimulated with varying amounts of electrical current and ongoing and consistent patient participation. In the setting of awake craniotomies, however, this is not always reliable. Moreover, stimulation is not without limitations. Discharges after stimulation have been found to occur in approximately 71% of all patients mapped (32). These discharges can induce seizures or provide misleading func-

tional responses from the distally stimulated cortex. Additionally, insufficient stimulation can lead to a missed identification of an appropriate eloquent site. In light of the current constraints for ECS mapping, an adjunct approach to defining motor related areas of cerebral cortex is the use of electrocorticographic signal changes associated with active regions of cortex (15).

Since 1929, it has been know that the brain generates oscillating electrical signals (16). These signals were originally recorded from the scalp using electroencephalography (EEG) and were subsequently detected directly from the surface of the brain by electrocorticography (ECoG). The fluctuations in the electrical activity of the brain oscillate in a broad range of frequencies. These frequencies have been categorized into three main functional groups as they relate to the sensorimotor cortex. Sensorimotor rhythms comprise the mu band (8–12 Hz), the beta band (18–26 Hz), and the gamma band (>30 Hz) (18, 31, 39). Mu and beta bands are thought to be produced by thalamocortical circuits, and they change in amplitude (i.e., signal magnitude measured in mV) in association with actual or imagined movements (14, 22, 30, 33). The higher frequencies in the gamma band are thought to be produced by smaller cortical assemblies and have also been found to change in amplitude relative to active or imagined motor movements (8, 21, 24). In general, the lower frequency bands of mu and beta tend to reduce their amplitude, also known as event related desynchronization, whereas the higher gamma band tends to increase in amplitude, also known as event related synchronization, when the region of cortex associated with the motor action becomes active (27, 28, 30).

The electrical activity of the brain is measured in mV using electrodes placed either on the surface of the scalp by EEG or the cortex by ECoG. The energy of this signal (power expressed as mV^2) can describe how that energy is distributed with regard to frequency. This is known as a frequency power spectrum. This is a useful method for discerning, with numerous signals at numerous different frequencies, system changes that occur from one state to another. Because the brain signals are composed of a broad range of frequencies and there can be different amplitudes at various frequencies, the alteration in amplitude can be expressed in the change in the energy or power of the given signal. Therefore, these changes associated with the active cortex can be described by the power for a given frequency band. A spectrum of frequency power reflects how the signal power varies across the entire range of frequencies. *Figure 1* shows an example in which the mu and beta bands show a power reduction, whereas the gamma band shows a power increase when the sensorimotor cortex becomes active.

These described frequency power changes associated with cortical activation could potentially provide a powerful tool in identifying and delineating regional areas of the motor cortex. For the purpose of motor mapping as it pertains to neurological surgery, the activated motor cortex could be identified by detection of the cortex regions that show spectral power changes associated with selected motor activities using a method of electrocorticographic frequency alteration mapping (EFAM). Demonstrating concordance between the sites identified by electrical stimulation and the regions of spectral power change demonstrate the possible future utility of EFAM as an adjunct method to improve the efficiency of identifying the motor cortex and allow for a higher resolution of defining the motor mosaic.

METHODS

To test the efficacy of the EFAM approach, we evaluated seven patients with intractable epilepsy who underwent placement of subdural grid electrodes for the purpose of seizure localization. All seven patients had extraoperative, electrocortical stimulation mapping performed to identify the motor cortex. Additionally, each of the patients performed overt motor hand and tongue tasks to identify associated frequency spectra power changes in regard to location, frequency, and manner of power change. The topographic distribution of cortical power changes, or EFAM maps, were then compared with those areas identified by ECS.

Patients

The study group consisted of seven patients (four men, three women) between the ages of 21 and 39 years with intractable epilepsy who underwent temporary placement of intracranial electrode arrays to localize seizure foci before surgical resection. Patients were either from University of Washington in Seattle, Washington, or Washington University in St. Louis, Missouri. The study was approved by the Human Studies Committee of Washington University Medical Center and the University of Washington Medical Center (*Table 1*). Invasive monitoring lasted for 7 to 14 days. During this period of time, all experiments and ECS were performed extraoperatively. All subjects had grid electrodes over sensorimotor cortex (three right, four left).

Experimental Setup

Experiments were conducted at two sites and were originally used for signal location and identification for the purposes of achieving electrocorticography-based brain-computer interface device control (19, 20). Signal acquisition was slightly different between the two institutions. At the University of Washington, Neuroscan Synamps2 amplifiers (Compumedics, El Paso, TX) were used during monitoring to record the signal from the grid electrodes. The leads were split as they exited from the head, with signals recorded in parallel to the clinical amplifiers. The signals were sampled at 1000 Hz and bandpass filtered (0.1–220Hz). At Barnes Jewish Hospital, signals were acquired in real-time from a local network after being acquired by an XLTech Acquisition computer (Oakville, Canada). The signals were sampled at 500 Hz and bandpass filtered (0.1–220Hz). In both cases, the utilized electrodes were platinum grid electrodes embedded in silastic sheets (range of dimensions, 60 × 80mm–80 × 80mm) and manufactured by Ad-Tech (Racine, WI). The number of electrodes per grid

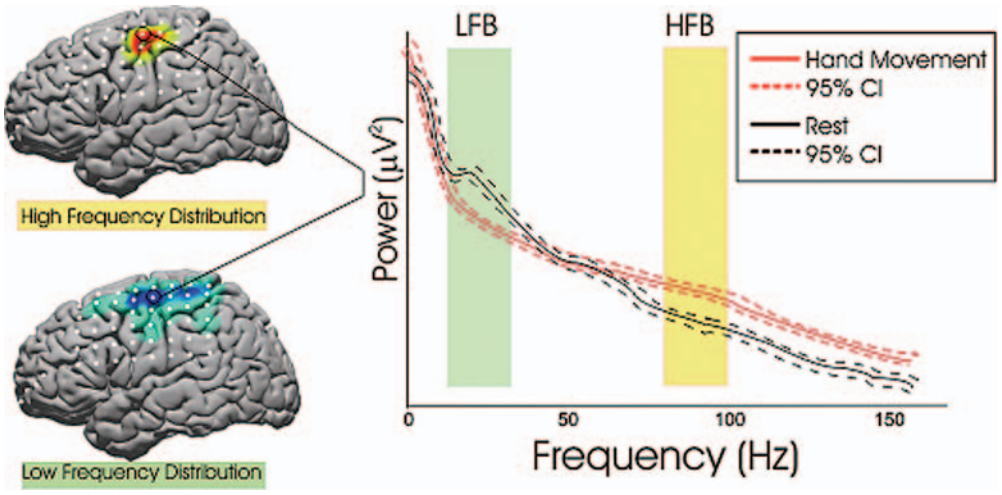

FIGURE 1. *Anatomic frequency distribution of electrocorticographic signal. Example of the variable frequency power alteration and spatial distribution for a given motor task. In this example, on the right side, power versus frequency is compared for a single electrode (*circled *in the two brains on the left) between the active condition of hand movement (*red line*) against rest (*black line*). The* dotted lines *are the respective 95% confidence intervals for each respective condition. For hand movement, there is a power decrease in the lower frequency range and a power increase in the higher frequencies. When specific 25 Hz frequency bands are chosen, the LFB (8–32 Hz,* green bar*) and HFB (76–100 Hz ,* yellow bar*); there is a different topographic distribution on the cortex (as shown in the two brains on the left). The LFB is more diffuse, whereas the HFB is more focal.*

ranged from 28 to 64. The electrodes were circular in shape and measured 4 mm in diameter, with 2.3 mm exposed, and were spaced 10 mm apart (center to center).

Stimuli

All cues for motor movement were delivered visually on a flat screen monitor in a 10 cm × 10 cm presentation window at a distance of 75 to 100 cm from the patient. Visual cues were presented using the BCI2000 (Wadsworth Center, Albany, NY) program (34). BCI2000 is a general-purpose system for data acquisition, stimulus presentation, brain-computer interfacing, and brain monitoring (34). It supports acquisition from a number of hardware devices, can process different types of brain signals, such as evoked potentials or frequency oscillations, and can relay the output of that processing to a variety of output devices. In the context of brain mapping, it supports programmable presentation of auditory and visual stimuli. BCI2000 associates the timing of these stimuli with the recorded ECoG signals, which facilitates offline analyses. A cue was given for the patient to perform either a hand task (repeatedly opening and closing the hand contralateral to the side where the grid electrodes were placed), or a tongue task (repeatedly protruding and retracting the tongue) for a period of 3 seconds (i.e., a trial). The patient was instructed before commencing the task to perform one of the two tasks when the appropriate cue was presented. The cue stated either "hand" or "tongue" on the screen as indication to begin moving that part of their body. When the word disappeared, they were to stop moving. The rest period between trials was also 3 seconds. The number of trials for each modality tested (a run) ranged between 30 and 75, depending on the patient's ability to participate. Motor screening sessions ranged from 5 to 30 minutes, with individual runs lasting from 2 to 10 minutes.

Analysis

For each timepoint, the data were referenced with respect to the signal mean computed from all channels recorded from the respective patient. The time segment from each 3-second trial that was used for data analysis consisted of an epoch starting at 0.5 seconds into the trial and ending at 2.0 seconds. This 1.5-second epoch was used for analysis of all trials regardless of sampling frequency (500 and 1000Hz for Washington University and University of Washington, respectively) or cue duration (certain subjects required prolonged cue duration to effectively participate). Because a standardized time was chosen within each epoch, there should be minimal confounding factors with regard to timing or cue duration. The power spectral density coefficients of each epoch were calculated using a fast Fourier transform. Fast Fourier transforms of 1 second in length were calculated using 0.25-second windows with 0.1-second step sizes, regardless of the sampling rate. A Hanning window was imposed on each data window to attenuate edge effects (12).

The power at each frequency for each epoch was normalized with respect to the mean power at that particular frequency across all the epochs from the run from which it was acquired. This flattened out the spectral landscape, which was necessary if intervals of the spectra were to be summed. Once normalized curves were calculated, the area under two selected 25 Hz-wide bands of the spectral curve were measured and summed. The two bands chosen were: 1) 8 to 32 Hz (low frequency band [LFB]): This is the classic mu and beta region associated with motor movement, and 2) 76 to 100 Hz (high frequency band [HFB]): This particular interval was chosen because it lies within the broad gamma band frequency power increase, was distant from the possible 60 Hz contamination from ambient power supply, and was low enough to not be attenuated by the low pass filter of the utilized amplifiers.

In each run, the number of rest epochs was randomly downsampled so that the number of rest and active epochs of each type were the same. In this manner, the 30 to 90 HFB epoch val-

TABLE 1. Patient summary[a]

Patient no.	Age (yr)/sex	Hand	Cognitive capacity	Grid location	Seizure focus
1	23/M	R	Normal	L frontotemporal	L temporal
2	35/F	L	Normal	L frontotemporoparietal	L temporal
3	25/M	R	Normal	L temporoparietal	L temporal
4	46/F	L	Normal	L frontal	L frontal
5	21/M	R	Normal	R frontoparietal	R parietal
6	38/M	R	Borderline (IQ = 70)	R frontal	R frontal
7	22/F	R	Normal	L frontal	L frontal

[a] R, right; L, left; IQ, intelligence quotient.

ues for each movement modality were compared with 30 to 90 HFB epoch values for rest. The same process was followed for the LFB values.

For each electrode, we compared the power spectra distribution of HFBs and LFBs for each motor modality with the corresponding distribution during rest intervals. To do this, we calculated the coefficient of determination (r^2) of the spectral power change with the given motor task when compared against rest. The r^2 is the percentage measure of how much variance in power corresponds to a given condition. Therefore, if the power increased at a certain frequency band with a motor task every time the motor task was performed, the correlation (r) would be 1 ($r = 1$), and the coefficient of determination would also be 1 ($r^2 = 1$). If the power decreased only 70% of the time that the motor task was performed, the correlation would be -0.7, and the coefficient of determination would be 0.49. Therefore, the r^2 value is always positive. The r^2 value was then defined as the weight a given electrode was assigned for the power change associated with a given motor task. As an example, if the r^2 value for tongue movement was 0.5, the weight assigned to that electrode site was 0.5 when summed with other electrode sites when looking at the data collectively. The r^2 value was also signed with a positive or negative value to reflect whether or not the relevant change in spectra was an increase or decrease in power for the motor modality when compared against rest. Separately, a *P* -value was also calculated using a balanced, one-way, analysis of variance with these same HFB and LFB power alterations. Each *P* value was Bonferroni corrected to account for multiple comparisons across channels, although they were done independently for HFB and LFB.

Anatomic Localization of Signal Change

X-rays were used to identify the stereotactic coordinates of each grid electrode (9), and cortical areas were defined using Talairach's coplanar stereotaxic atlas of the human brain (37) and a Talairach transformation database (http://ric.uthscsa.edu/projects/talairachdaemon.html). We obtained a three-dimensional cortical brain model from the AFNI SUMA web site (http://afni.nimh.nih.gov/afni/suma). Stereotactically defined electrode locations were then mapped to this standardized brain model. Using these locations, activation plots were created for each modality in each patient on a template cortex. This was done for both HFB and LFB using a multi-step process. First, electrodes with corrected *P* values for the associated task greater than 0.05 were discarded from the mapping interpolation procedure. Next, a spherical Gaussian kernel was centered on all remaining electrode locations with a width of 5 mm and variance of 25 mm. A spherical Gaussian kernel is a weighting function that declined in three-dimensional space with the peak weight at the center of the sphere and the decline of the weight decreasing in a normal Gaussian distribution. The purpose of the Gaussian kernel was to smear singular point data to a more confluent distribution. This allowed for the smoothing or averaging of data identified at multiple singular electrode positions across a template brain cortex. Because the variance was defined as 25 mm, a full standard deviation was encompassed in the visible 5 mm diameter of the kernel. This was the optimal size to allow for summation across electrodes spaced 10 mm apart. Each of these Gaussian kernels was then multiplied by the assigned weight, which was derived from the signed associated r^2 value, with the corresponding electrode and the given motor modality. These Gaussian kernels were then linearly superimposed to find the activation at each point on the template cortex for each category, namely, by frequency band (LFB or HFB) and by motor task (hand or tongue). The scaling of maximum and minimum on each map was performed with respect to the maximum absolute weight.

Separate from the experiments described above, each patient underwent stimulation mapping to identify the motor cortices as part of his or her clinical care. In this mapping, 1 ms 5 to 10 mA current pulses were passed through paired electrodes to induce sensation and/or evoke motor responses. The experimental results described above were collated with these anatomic and functional mapping data. Of note, only stimulations that produced motor effects were noted (i.e., sensory and speech responses were not considered).

Comparison of ECS and EFAM Maps

For each patient, ECS positive electrodes (sites that induced a motor response) and electrodes that demonstrated a significant spectral power change were identified and compared according to motor modality. We assessed the significant hand and tongue LFB and HFB electrode groups' sensitivity and specificity in identifying the ECS positive electrodes (the true

positive sites) which elicited a corresponding motor response. The sensitivity was determined by dividing the number of true positives (ECS positive electrodes, which were also either LFB or HFB positive, by the true positives plus the number of false negatives, which was either the significant electrode identified by the LFB or HFB, which did not correspond to an ECS identified site). The specificity was determined by the number of true negatives (electrodes that were both ECS and LFB, or HFB negative) divided by the true negatives plus either the LFB or HFB positive electrodes that did not correspond to an ECS positive electrode. An example is shown below:

General Table for Determining Sensitivity and Specificity

	True+	True−
Test+	A	B
Test−	C	D

Sensitivity = A/A+C
Specificity = D/B+D

Example: LFB sensitivity and specificity to hand

	ECS+	ECS−
LFB+	187	54
LFB2−	3	185

Sensitivity = 18/18+3 = 0.857 = 85.7%
Specificity = 185/54+185 = 0.774 = 77.4%

Additionally, χ^2 analysis was used to assess whether or not the HFB and LFB electrode distribution for hand and tongue motor movement significantly overlapped with corresponding ECS positive motor response electrodes. Because identification of eloquent cortex requires bipolar (two electrode) stimulation, we also assessed the HFB and LFB electrode groups' sensitivity and specificity to identify at least one of the electrode pairs, assuming the electrode pairs were non-overlapping and in a horizontal orientation. The choice for the non-overlapping horizontal orientation was because it most closely reflects the method for which patients are extraoperatively mapped, namely, one horizontal electrode pair at a time. Finally, we also qualitatively compared the distribution and location of the ECS positive electrodes to the EFAM maps superimposed on a standardized brain model.

RESULTS

The correlation between the two modalities of cortical mapping, ECS and EFAM, were compared in several ways. Because the cortex involved with the motor response is generated by stimulation from the current between the electrode pair, we assessed the correlation of significant frequency power alteration in regard to the pair of stimulated electrodes and to the individual electrodes. This correlation for both paired and individual electrodes was then further subdivided into motor response (hand and tongue movement) and HFB and LFB. Of the seven patients in this study, five had ECS-induced tongue movements and six had ECS-induced hand movements. For each motor response, both individual and paired electrodes were compared with the electrode sites associated with statistically significant HFB and LFB spectral power change. The correlation for a given motor response with ECS was considered in relation to the HFB, LFB, and both LFB and HFB taken together (i.e., a given electrode demonstrates LFB and/or HFB signal change is EFAM positive) (*Table 2*).

When the paired electrodes associated with stimulated motor responses were compared with EFAM positive sites, both hand and tongue movements elicited were closely coupled with findings of frequency alteration. In general, the LFB tended to be

TABLE 2. Electrode analysis[a]

Electrodes summary	Tongue totals	Hand totals
Total no. of electrodes	196	260
Electrodes with significant HFB power change	25	34
Electrodes with significant LFB power change	47	72
Electrodes with either significant LFB or HFB power change (EFAM +)	56	83
No. of electrodes producing motor response	18	21
Electrodes with significant HFB power change and motor response	9	9
Electrodes with significant LFB power change and motor response	12	18
Electrodes with either significant LFB or HFB power change and motor response	14	18
No. of electrode pairs producing motor response	9	11
No. of electrode pairs producing motor response of which one electrode corresponds to significant HFB power change	8	8
No. of electrode pairs producing motor response of which one electrode corresponds to significant LFB power change	8	11
Electrodes stimulation pairs with either significant LFB or HFB power change and motor response (EFAM +)	9	11

[a] HFB, high frequency band; LFB, low frequency band; EFAM, electrocorticographic frequency alteration mapping.

TABLE 3. Summary of statistical analysis[a]

Frequency band	Tongue		Hand	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Single electrodes				
LFB	66.7	80.3	85.7	77.4
HFB	50.0	91.0	42.9	89.5
EFAM+	77.8	76.4	85.7	72.8
Electrode pairs				
LFB	88.9	82.6	100.0	79.0
HFB	88.9	94.9	72.7	92.4
EFAM+	100.0	78.6	100.0	74.4

[a] LFB, low frequency band; HFB, high frequency band; EFAM, electrocorticographic frequency alteration mapping.

more sensitive and the HFB tended to be more specific. Explicitly, LFB for ECS-elicited tongue movement was 88.9% sensitive and 82.6% specific; for the HFB, it was 88.9% sensitive and 94.9% specific. For ECS-induced hand movement, the LFB was 100% sensitive and 79.0% specific; and the HFB was 72.7% sensitive and 92.4% specific. When the HFB and LFB were taken together (HFB and/or LFB signal alteration at a given electrode), the EFAM-positive sites had 100% sensitivity and 78.6% specificity for identifying ECS-positive electrode pairs for inducing tongue movement, and a 100% sensitivity and 74.4% specificity for identifying ECS-positive electrode pairs for inducing hand movement.

When the electrodes used for stimulation were taken individually for comparison against significant frequency power alteration, the sensitivity for both tongue and hand movement dropped substantively in sensitivity and only slightly in specificity. In particular, for ECS-induced tongue movement, the LFB was 66.7% sensitive and 80.3% specific, and the HFB was 50.0% sensitive and 91.0% specific. For ECS-induced hand movements, the LFB was 85.7% sensitive and 77.4% specific, and the HFB was 42.9% sensitive and 89.5% specific. For the EFAM-positive sites, there was 77.8% sensitivity and 76.4% specificity to identifying ECS-positive electrodes for inducing tongue movement, and 85.7% sensitivity and 72.8% specificity for identifying ECS-positive electrodes for inducing hand movement.

The distributions of both electrode sites with either significant LFB or HFB power alteration were compared with the distribution of the ECS-positive electrodes using the χ^2 test. Both the LFB and HFB groups were found to significantly overlap with the ECS-positive distribution for both hand and tongue (tongue: LFB $\chi^2 = 19.8$, $P < 0.001$; HFB $\chi^2 = 24.7$, $P < 0.001$; hand LFB $\chi^2 = 29.2$, $P < 0.001$, HFB $\chi^2 = 17.8$, $P < 0.001$).

Figures 2 to 5 demonstrate the grid electrodes and the regions of cortex identified on the template brain that show significant power alteration with respect to the LFB or the HFB in terms of either hand or tongue movement. In the majority of electrodes found to demonstrate statistically significant ($P < 0.05$) power alterations, both tongue and hand movement induced a power depression in the LFB and power increase in the HFB. The cortical topographical distribution for the significant LFB power changes tended to be more diffuse than the more focal distribution of significant power changes in the HFB. Additionally, the cortical distribution of the power change in both frequency bands was distinct between motor modalities for the subjects who had both hand and tongue motor tasks mapped (Patients 1, 3, 4, and 7).

For both the LFB and HFB, this was most prominent in Patients 1, 3, and 4, in whom hand regions tended to be superior to tongue regions along the Rolandic cortex. The spatial discrimination between hand and tongue was more pronounced with HFB because of its more constrained cortical distribution. Patient 7 showed only task-specific differences in the LFB. The HFB power fluctuations did not demonstrate statistical significance.

DISCUSSION

Over the past decade, significant scientific attention has been given to understand how electrical signals, such as EEG and ECoG, correlate to motor function and motor intention. This work has primarily been done in the context of neurophysiological and psychological experiments, and developing brain-computer interface systems that can identify a signal from sensorimotor cortex using that signal for a type of overt device control (20). These experimental approaches have led to our current understanding of sensorimotor rhythms. Sensorimotor rhythms comprise mu (8–12 Hz), beta (18–26 Hz), and gamma (>30 Hz) oscillations (18, 31, 39). These are also referred to as the mu, beta, and gamma bands. As mentioned earlier, the lower frequencies of mu and beta are thought to be produced by thalamocortical circuits, and they change in amplitude in association with actual or imagined movements (14, 22, 30, 33). In general, these LFBs tend to have a wide cortical distribution. Higher frequencies (>30 Hz), or gamma bands, are thought to be produced by smaller cortical circuits (24). The gamma band tends to have a more cortically focal anatomic distribution. Based on EEG oscillations, BCIs have focused exclusively on mu and beta rhythms. This is because of several factors. The low frequency mu and beta bands are broadly distributed over the cortex and are, therefore, appreciable on the surface of the scalp (29). In contrast, high frequency gamma rhythms, as well as mu and beta rhythms, are prominent in ECoG during movements (14, 24, 29, 33). The ECoG signal has been known to be a more robust signal than EEG. Its magnitude is typically five times larger (0.05–1.0 versus 0.01–0.2 mV for EEG) (2), its spatial resolution (i.e., electrode spacing) is much finer (0.125 versus 3.0 cm for EEG) (10, 36), and its frequency bandwidth is significantly higher (0–200 Hz versus 0–40 Hz for EEG). Until recently, the signal was assumed to be very similar to that of EEG in regard to the amount and type of information it could convey. However, this is not true; the signal itself was found to be substantially different. On a functional level, several studies have revealed that higher frequencies carry highly specific and anatomically focal information about cortical processing in regard to speech, motor

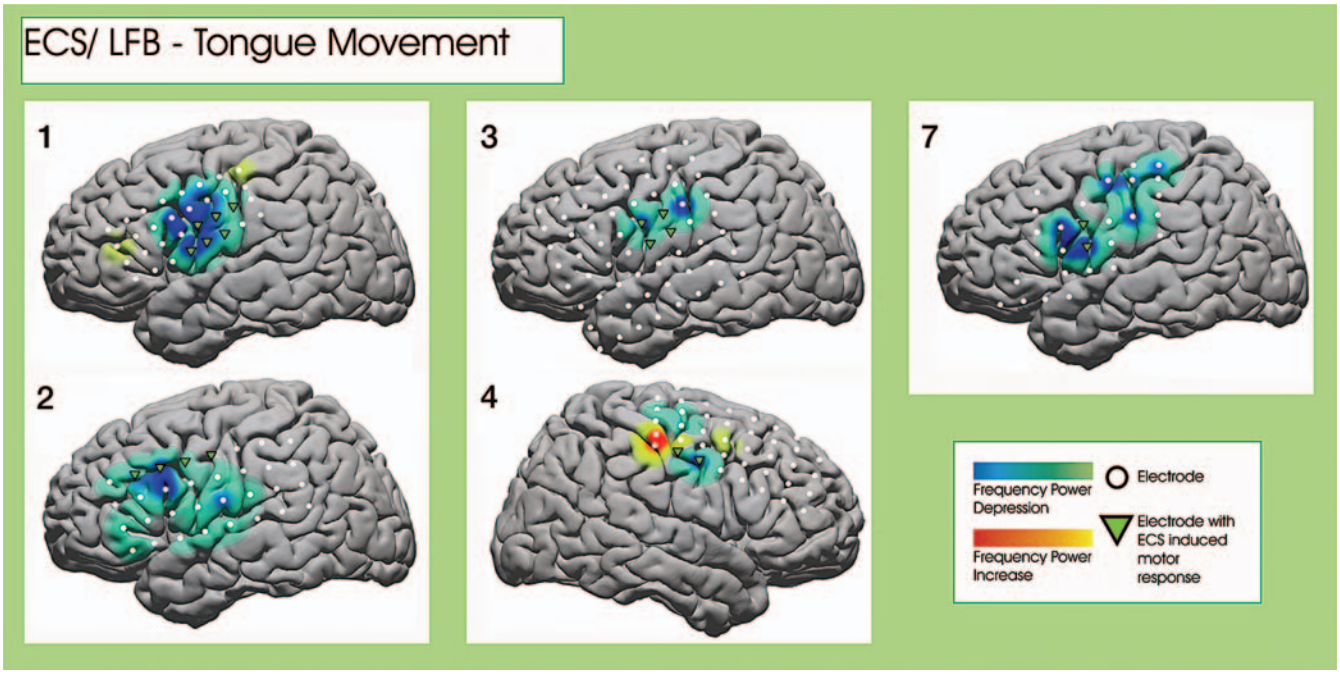

FIGURE 2. *Comparison of stimulation mapping and LFB power alteration for tongue movement. The figure demonstrates the grid electrodes and the regions of cortex identified on the template brain which demonstrate significant LFB power alteration in context to the electrodes that induced tongue movement with ECS for patients 1, 2, 3, 4, and 7. The values are normalized to maximum increase or decrease, such that an activation of 0 is always* gray, *with maximum increase as* red, *and maximum decrease as* blue, *scaled to the highest absolute value in the activation map. Maps that appear purely* gray *had no significant change with the stated motor modality. Electrode locations are shown as* white dots. *Electrodes where clinical stimulation produced a motor effect of the type being mapped are shown with* green triangles. *In general, tongue movement induced a broad cortical power depression in the LFB which correlated with regions identified with ECS.* ECS, *electrocortical stimulation;* LBF, *low frequency band;* HFB, *high frequency band.*

movements, and motor intention (6–8, 21, 35). Additionally, these higher frequencies conferred significant advantages in achieving a more rapid user control of a brain-computer interface (21). Given the emerging understanding of electrocorticography, the variable anatomic distributions of various frequency bands, and the rich nature of gamma frequencies, we formerly set out to evaluate how useful these various frequency bands would be in identifying functional motor cortex when compared against the current gold standard of ECS.

This work confirms the previously proposed notion that ECoG mapping could be a useful tool in mapping the human cortex (6–8, 21, 27, 30). Defining regions of the motor cortex through electrocorticographic frequency power alterations with motor movements correlates well with defined methods of cortical motor mapping through ECS. We find this with two different motor tasks providing topographically distinct sites on the cortical surface, which correspond with ECS sites. Furthermore, parsing the frequency alterations into HFB and LFB provides additional information. The LFB encompasses the classically defined mu and beta bands, which are thought to represent thalamocortical circuits (27, 30). Qualitatively, these low frequency power depressions associated with hand and tongue motor tasks were found to be topographically diffuse, whereas the HFB power increases (postulated to represent smaller cortical-cortical circuits) were found to be more spatially focal. This is consistent with previously described literature (8, 30). Moreover, this anatomic data was acquired without the difficulties associated with stimulation (i.e., after discharges and seizures), and the whole array can be interrogated in minutes. This EFAM method provides a rich amount of useful and low risk information in regard to anatomic cortical location associated with a given motor task. Given the close correlation of the EFAM with ECS maps and its low risk and short time requirements for information accrual, EFAM could be a powerful adjunct method for delineating the cortex in conjunction with ECS.

There are several potential strategies one could use to capitalize on the information provided by EFAM techniques to complement those of standard intra- and extraoperative ECS mapping methodologies. The differential spatial distribution of the LFB and HFB power alterations provide alternate priority maps that can be used to guide where one should apply bipolar stimulation. The broad topography of LFB power depression (hence higher sensitivity and lower specificity) can provide a method for creating a general priority map for electrodes to stimulate, although the more focal HFB power increase (less sensitive and more specific) provides a highest probability starting point within the general map to localize the functional cortex with ECS. Moreover, the focal distribution of

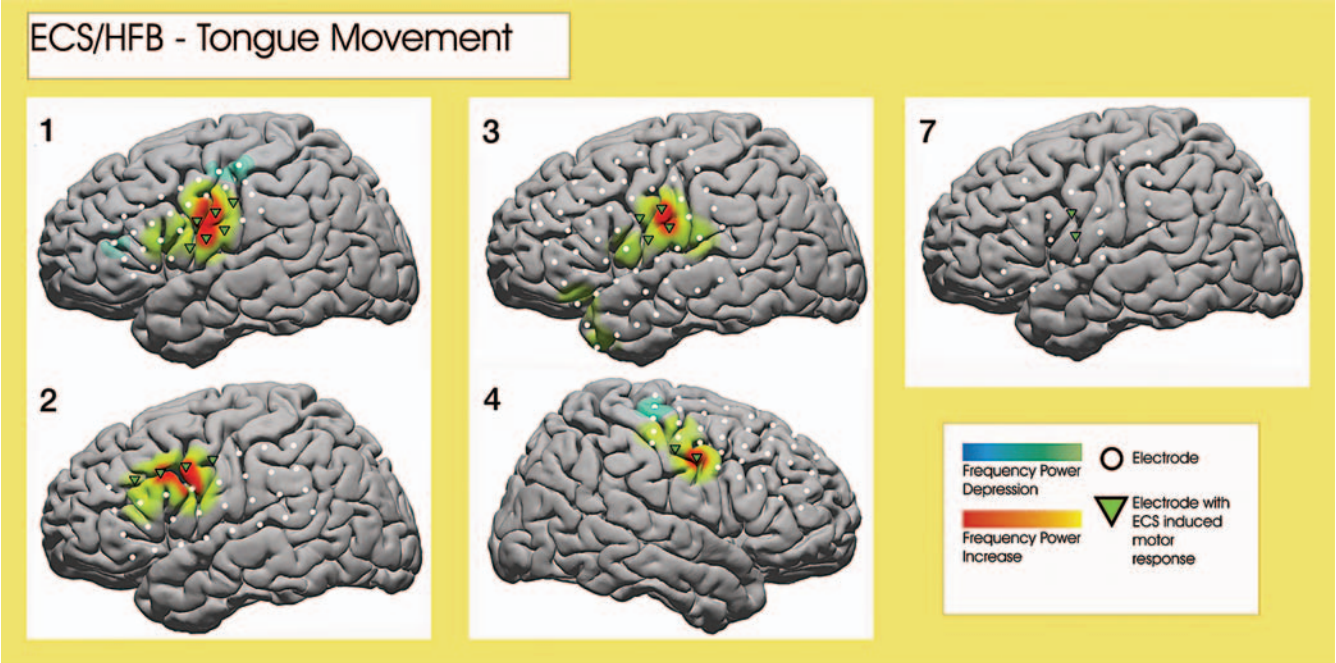

FIGURE 3. *Comparison of stimulation mapping and HFB power alteration for tongue movement for Patients 1, 2, 3, 4, and 7. The grid electrodes and the regions of cortex identified on the template brain demonstrate significant HFB power alteration in context to the electrodes that induced tongue movement with ECS. In general, tongue movement induced a more focal region of cortical power increase in the HFB, which correlated closely with regions identified with ECS. Of note, Patient 7 did not show statistically significant HFB power alteration.* ECS, *electrocortical stimulation;* LBF, *low frequency band;* HFB, *high frequency band.*

HFB power alteration can more efficiently refine stimulation results once the functional cortex is identified with bipolar ECS. From the results, HFB power increase, when correlated with electrodes positive for inducing a motor response predominantly often correlated with only one of the electrodes of the pair that would induce a motor response with ECS (versus correlating with both electrodes). Because the motor cortex is identified by passing electrical current from one electrode to the other, the anatomic location of that particular functional region is defined by the two electrodes involved in stimulation. Although one can define the relevant electrode of a bipolar pair most closely associated with functional cortex by using multiple bipolar combinations, this can be cumbersome and time consuming. From these two electrodes, the location of the functional cortex can be further resolved to a single electrode by demonstrating which of the electrodes shows significant HFB power increases.

Additionally, EFAM demonstrated areas of cortical activation that were not associated with positive ECS-induced motor responses. This is most notable in *Figures 4* and *5* with regard to the LFB power suppression being more cortically diffuse than the sites identified with ECS. For the lower frequencies, this is consistent with the previously reported literature, in which low frequencies are thought to represent broader thalamocortical circuits that have a wider cortical distribution when associated with motor movements (27, 30). In regard to the higher frequencies that differed from ECS locations, some of these findings may correspond with the associated nonmotor processes related to actual motor function, such as sensation or other non-motor associated functions (as has been demonstrated with functional magnetic resonance imaging) (25). Currently, the relevance of these sites to preserving function is not clear and will require further exploration. The ECS-negative and EFAM-positive regions of cortex may shed light on the study by Haglund et al. (11), who found that the most significant factor in preserving function was maintaining a margin of 1 cm around regions identified as ECS-positive electrodes. The EFAM technique may provide a more objective and empiric method of defining what is relevant and non-relevant around those ECS-positive sites when resection is considered. Finally, EFAM may provide another useful tool, in addition to somatosensory-evoked potentials, when cortical stimulation produces no results in identifying the sensorimotor cortex.

The use of r^2 weighted spherical kernels applied to each electrode, such that multiple electrode data can be summed and projected on a template model brain, improves one's ability to qualitatively appreciate the relationship of the contributions of various electrodes (hence cortical surface) to a given motor task. Rather than each individual electrode site being associated with a given motor task as only positive or negative, the

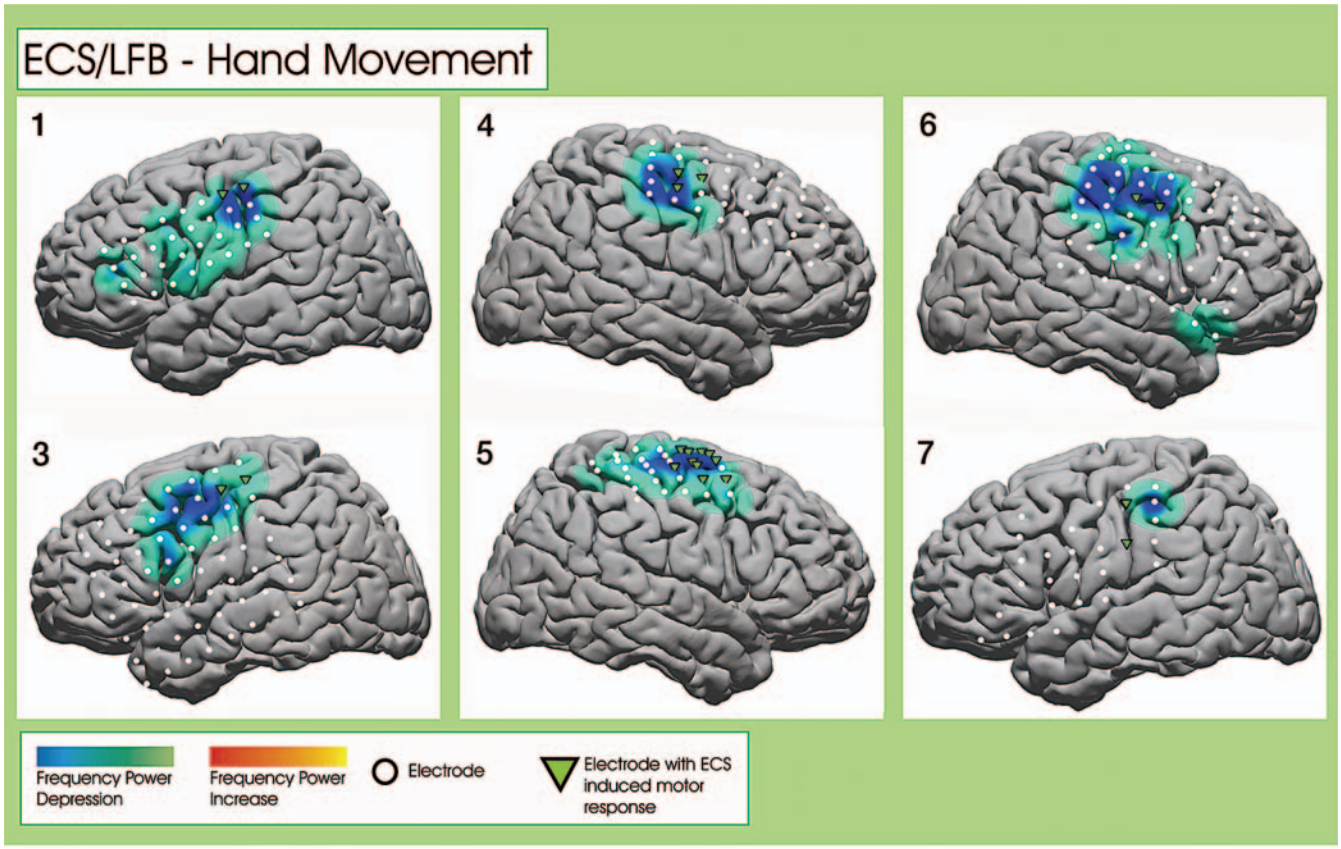

FIGURE 4. *Comparison of stimulation mapping and LFB power alteration for hand movement for Patients 1, 3, 4, 5, 6, and 7. The grid electrodes and the regions of the cortex identified on the template brain demonstrate significant LFB power alteration in terms of the electrodes that induced hand movement with ECS. In general, hand movement induced a broad cortical power depression in the LFB which overlapped with regions identified with ECS.* ECS, *electrocortical stimulation;* LBF, *low frequency band;* HFB, *high frequency band.*

weighted summation of statistically significant power spectra change allows one to associate a given cortical site in a more graded fashion. It allows for a comparison between relevant sites (i.e., Electrode 4 is more closely associated with hand movement than Electrode 5). Although a Talairach template brain was used in this series, one could also adapt this technique to have the data projected onto a three-dimensional reconstruction of a patient's brain taken from magnetic resonance imaging or computed tomographic scans. This compilation of single electrode data onto a template may allow one to have a more intuitive appreciation of the cortex associated with relevant function by its easy viewable context. Although not tested in this series, EFAM could potentially be useful when the motor cortex does not follow normal anatomic configurations.

This method should also be considered in light of other electrophysiological methods of site identification, such as event related potentials (ERPs), functional imaging modalities, such functional magnetic resonance imaging, and magnetoencephalography. In the past, ERPs have been used to identify sites of cortical activation associated with discrete motor events (14, 22, 23). When ongoing EEG or ECoG is averaged, time-locked to stimulus, or response events, the resultant waveforms are referred to as ERPs. The ERPs reflect discharges from large populations of neurons which are linked to specific aspects of sensory and cognitive processing (38). The advantage of identifying frequency power alterations as a method that is distinct and useful for brain mapping compared with ERP is twofold. First, ERPs average all of the frequency spectra together and then identify a significant change from that average. EFAM looks at the high and low frequencies, which seem to give different types of anatomic information. Therefore, EFAM has more information available to the user than ERPs, which combine this information. Second, for ERPs to be useful, they require strict time-locked matching of the event with the change in averaged signal. EFAM, although it still requires the active and rest conditions to be identified, is somewhat more flexible. Because the subject has 3-second trials of rest and activation, and the data taken from those trials are the central 1.5 seconds, versus a singular discrete event with ERPs, the adherence for strict time locking is less strin-

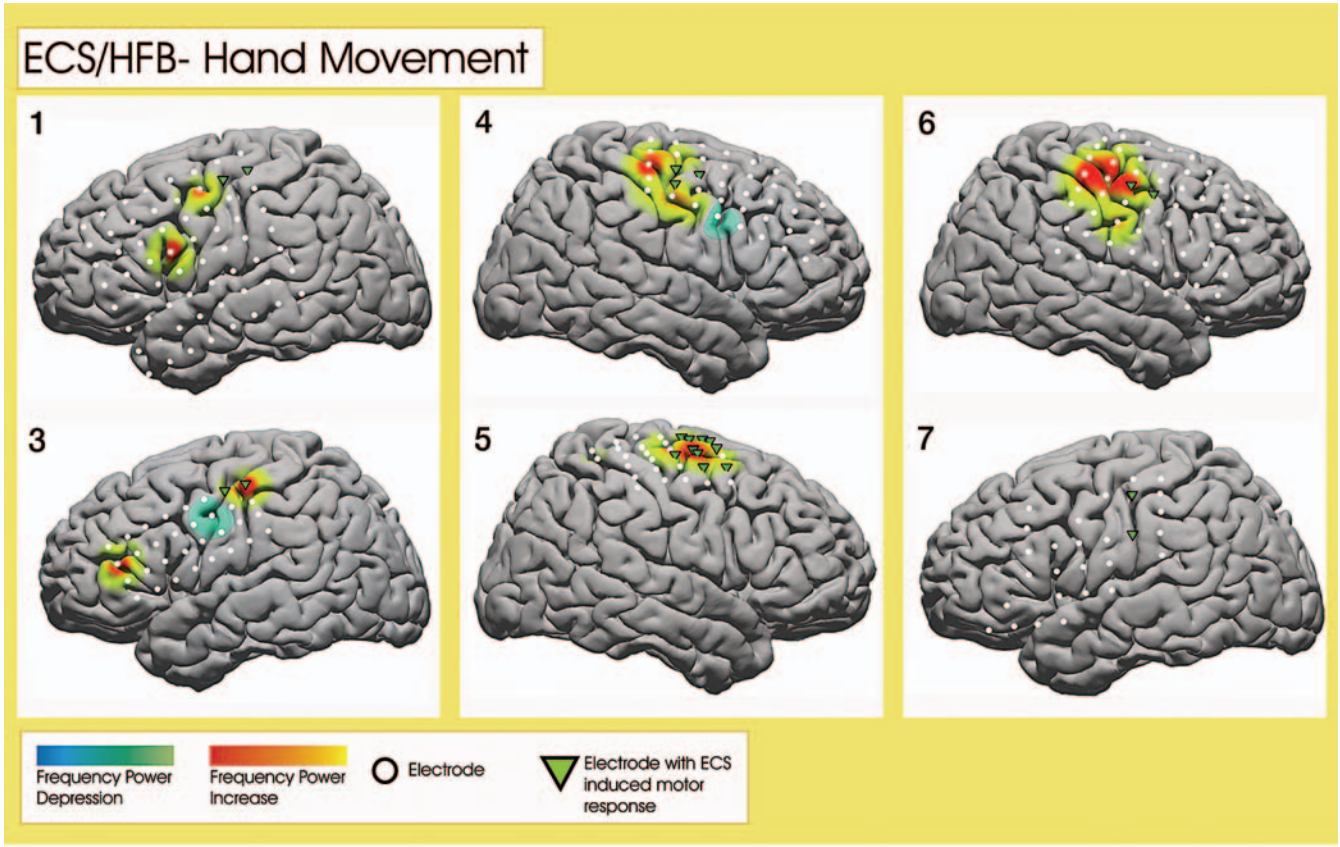

FIGURE 5. *Comparison of stimulation mapping and HFB power alteration for hand movement for Patients 1, 3, 4, 5, 6, and 7. The grid electrodes and the regions of cortex identified on the template brain demonstrate significant HFB power alteration in terms of the electrodes that induced hand movement with ECS. In general, hand movement induced a more focal region of cortical power increase in the HFB which correlated closely with regions identified with ECS. Of note, Patient 7 did not show statistically significant HFB power alteration.* ECS, *electrocortical stimulation;* LBF, *low frequency band;* HFB, *high frequency band.*

gent. With respect to magnetic resonance imaging and magnetoencephalography, these techniques are not easily used in the setting of ongoing extraoperative invasive monitoring or during awake craniotomies. This is because of the large infrastructure requirements required for both devices and the interference produced by electrodes in the case of invasive monitoring.

The results of this study, although preliminary, are an exciting entry into the feasibility of this modality as a possible new and useful technique for brain mapping. There are some caveats worth noting in regard to this methodology and its future study. This study compared normal cortex in regard to power frequency alterations and electrocortical stimulation. The reliability of EFAM activation and their mapped distributions will require a higher number of patients and more prolonged testing in given patients to more definitively demonstrate the stability and reproducibility of these findings in patients over time and across subjects. EFAM was not used around and in regions involving pathological tissue such as a tumor or arteriovenous malformation. How these lesions will affect the signal when pathological lesions encroach on or in motor tissue has yet to be determined. Additionally, EFAM and its association with functional outcomes and how one should tailor a given resection in light of these findings remain uncertain and will require further study with a higher number of subjects to both establish and validate this method for future practical usage. Also of note, this technique, as with ECS, will require continued patient participation. However, because the electrodes can be interrogated in parallel rather than in series, as is required with ECS, the time should theoretically be reduced. This time reduction, however, has not been explicitly tested. Finally, to identify eloquent cortex, both modalities require that the electrode arrays actually be over the true anatomic sites for appropriate identification.

In conclusion, the findings of this study suggest a useful potential adjunct technique to standard ECS methods for motor mapping. In the future, EFAM may provide the possibility of a rapid and more efficient method of identifying these and other eloquent regions of the cortex.

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COMMENTS

In this study, the authors sought to augment localization of the eloquent cortex using a frequency-based analysis of electrocorticographic subdural recordings from activated regions of the motor cortex. This method is proposed as an adjunct to existing electrical cortical stimulation (ECS) techniques. The authors examine the usage of electrocorticographic frequency alteration mapping (EFAM) for functional mapping of structurally normal motor cortex in seven patients with pharmacoresistant focal epilepsy undergoing routine extraoperative invasive recordings and ECS mapping. All subjects were instructed to perform overt hand and tongue motor tasks. Concomitant frequency power changes with motor movements were examined with regard to location and degree of concordance with the results of ECS.

Similar to previous studies, the authors observed that low frequency bands (LFB = 8–32 Hz; mu and beta rhythms) tend to show a topographically diffuse power reduction (LFB power depression) in relationship to hand and tongue motor tasks, whereas high frequency bands (HFB = 76–100 Hz) exhibit more focal power increases with cortical activation. The authors conclude that the differential spatial distri-

bution of LFB and HFB power alterations in relationship to motor tasks can be used to complement ECS mapping of the motor cortex. Therefore, EFAM may help identify the highest probability cortical region before applying bipolar stimulation.

It should be noted that these results are preliminary. Further studies are needed to establish and/or validate whether or not these changes are reproducible across a larger number of subjects with structurally normal anatomy, as well as subjects with lesions encroaching on the motor cortex. Finally, the significance and clinical relevance of EFAM-positive areas in the absence of ECS-induced motor responses remain under exploration.

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The authors present the new technique, electrocorticographic frequency alteration mapping, for identifying the functional cortex by using the analysis of frequency changes in the spontaneous electrocorticogram when the patient performs a functional task, such as moving the tongue or the hand. They also focused on the analysis of certain frequencies within the electrocorticography (ECoG) (high- and low-frequency bands) and checked for the change in power of these frequency bands during activation. The description of the technique contains a large number of technical terms, both for the electrophysiological aspects and the methodology to identify changes in the ECoG, which will be unfamiliar to a typical neurosurgeon. I do not expect a normal neurosurgeon to know what the "co-efficient of determination" is. Likewise the definition of a "spherical Gaussian kernel" will have to be read at least twice to be completely understood. The technologies used here imply a lot of methodological traps, and as reviewers, we enjoyed the dialogue with the authors during the reviewing and revision process. The authors have managed to nicely explain most of these very unfamiliar technical terms. The basic message of this article is that the authors feel they are able to demonstrate a correlation with the motor areas, which could be defined by traditional cortex stimulation when using this technique of electrocorticographic frequency alteration mapping. Although it was only tried in seven patients, the authors have demonstrated a certain concordance between the classic stimulation paradigm and the spectral power changes, which seems to demonstrate a possible usage of their technique as an additional method of identifying the motor cortex.

One reason to try this technique rather than the classic, standard direct cortical stimulation is because of certain disadvantages of intraoperative cortical stimulation that are usually not prominently indicated by its users, such as the appearance of after discharges, which is now given to 71% of all patients mapped and have the necessity for "ongoing and consistent patient participation." Having an alternate technique, which is not frequently inducing after discharges with the potential for induced seizures, is therefore relevant. Addressing this problem with this new approach is a good idea, and the authors have also been cautious not to overemphasize their findings. The authors should be congratulated on an innovative approach and a carefully conducted study using a complicated methodology to assess their results in a careful and self-critical way.

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Localized changes in the ECoG power spectrum during motor tasks are well recognized and reproducible. Leuthardt et al. have demonstrated these changes in a small group of grid-implanted patients, correlating their observations with conventional ECS using the same grid electrodes. The study is well done and provocative.

As a means of functional mapping the surgical patient, this methodology, for good reasons, warrant further exploration, not least of which is the potential efficiency relative to cortical stimulation. Used in combination with cortical stimulation, such as in directing more focused stimulation, as the authors suggest, this technique could be implemented now. However, as the authors also note, the full implications of this technique's findings with respect to decisions to resect or not to resect still need to be investigated and understood.

The history of understanding functional localization in the brain encompasses an evolution from the lesions of nature's own experiments (e.g., traumatic injury, stroke, tumor) to investigative interventions that either stimulate or temporarily inhibit tissue (e.g., electrical stimulation), and more recently, to non-interfering observations of either normal or abnormal brain through the remarkable technologies of advanced neuroimaging. Positron emission tomography, functional resonance imaging, and magnetoencephalography have contributed information both confirmatory of prior findings but also different in important ways. More sophisticated signal processing and analysis of ECoG recording are providing similar observational data. In their implication of additional areas in a given task, and their demonstration of distributed networks, rather than simpler, discrete areas, these methods suggest what tissue may be sufficient but not necessarily essential for execution of a given function.

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