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Decoding native cortical representations for flexion and extension at upper limb joints using electrocorticography

Tessy M. Thomas^{1,*}, Daniel N. Candrea^{1,*}, Matthew S. Fifer², David P. McMullen³, William S. Anderson⁴, Nitish V. Thakor^{1,5}, and Nathan E. Crone⁶

¹T. M. Thomas, D. N. Candrea, and N.V. Thakor are with Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 21205, USA. (tlal1@jhmi.edu)

²M. S. Fifer is with the Research and Exploratory Development Department, Johns Hopkins University Applied Physics Laboratory, Laurel, MD 20723, USA.

³D. P. McMullen is with the Division of Translational Research, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892, USA.

⁴W. S. Anderson is with the Department of Neurosurgery, Johns Hopkins University, Baltimore, MD 21205, USA.

⁵N. V. Thakor is also affiliated with the SINAPSE Institute, National University of Singapore, Singapore.

⁶N. E. Crone is with the Department of Neurology, Johns Hopkins University, Baltimore, MD 21205, USA.

Abstract

Brain-machine interface (BMI) researchers have traditionally focused on modeling endpoint reaching tasks to provide control of neurally-driven prosthetic arms. Most previous research has focused on achieving endpoint control through a Cartesian-coordinate-centered approach. However, a joint-centered approach could potentially be used to intuitively control a wide range of limb movements. We systematically investigated the feasibility of discriminating between flexion and extension of different upper limb joints using electrocorticography (ECoG) recordings from sensorimotor cortex. Four subjects implanted with macro-ECoG (10 mm spacing), HD-ECoG (5 mm spacing), and/or micro-ECoG arrays (0.9 mm spacing, 4×4 mm coverage), performed randomly cued flexions or extensions of the fingers, wrist, or elbow contralateral to the implanted hemisphere. We trained a linear model to classify six movements using averaged high-gamma power (70–110 Hz) modulations at different latencies with respect to movement onset, and within a time interval restricted to flexion or extension at each joint. Offline decoding models for each subject classified these movements with accuracies of 62–83%. Our results suggest that widespread ECoG coverage of sensorimotor cortex could allow a whole limb BMI to sample native cortical representations in order to control flexion and extension at multiple joints.

*These authors are co-first authors of this publication.

Keywords

Classification; Electrocorticography; Extension; Flexion; Upper Limb

I. INTRODUCTION

Current research in motor brain-machine interfaces (BMI) aims to restore function to patients with upper limb paralysis. Several groups have primarily used microelectrode arrays (MEAs) to record from single neurons in the sensorimotor cortex of these patients, and to provide users neural control of maneuvering an end-effector in 2D or 3D coordinate space or shaping a prosthetic hand into specific configurations [1–6]. Since these arrays only cover a small portion of the cortical surface, they do not capture neural activity across all cortical regions that may be important for naturalistic control of upper limb movements. BMIs using these arrays require extensive training whereby users map single-unit firing rates onto individual degrees of freedom of end-effectors.

Electrocorticography (ECoG) provides more extensive coverage of the cortical surface than MEAs and better signal quality than noninvasive neural recording modalities (e.g., EEG, fNIRS). While some studies have shown that ECoG can also be used to develop a BMI, most of these studies have not provided users much functionality beyond cursor control or simple reaching and grasping movements that involve simultaneous control of multiple joints [7–12]. Bundy et al. [13] have provided the most evidence showing ECoG can be used to perform endpoint control in a 3D cube-oriented workspace. Using ECoG to provide control of individual degrees of freedom (DoFs) at different joints could expand on the repertoire of movements controlled with previous models. Also, because ECoG arrays could capture native neural representations more comprehensively (as opposed to consistently training neural signals using MEAs), an ECoG-based decoding model would allow more intuitive and flexible control.

Only a few studies have examined the neural representations of distal and proximal joints to explore their potential utility in controlling the upper limb, and they have found that movement kinematics of upper limb joints have discriminable neural correlates. Two groups have shown that it is possible to reconstruct joint kinematics of the hand, wrist, and arm moving simultaneously during reach and grasp movements from single-unit firing rates of neurons in the primary motor cortex (M1) of non-human primates (NHPs) [14,15]. Similarly, Nakanishi et al. [16] showed through offline analysis that ECoG recordings from sensorimotor cortex in humans can be used to infer wrist and elbow positions and joint angles during object transport motions within a bounded workspace.

Other studies have compared the neural representations of flexion and extension movements about a single joint. Using single-unit recordings from the precentral and postcentral gyri of NHPs, one group showed that some neurons were active for either flexion or extension about the elbow, while other neurons were active for both movements [17,18]. Later studies have also investigated representations of flexion and extension of the fingers using fMRI [19], MEAs [20], and ECoG [21]. Additionally, Yanagisawa et al. [22] showed that flexion and extension of the elbow and fingers can be decoded using ECoG recordings from patients

with and without motor impairments. This provided preliminary evidence that ECoG-based classification of flexion and extension about different joints was possible and could be used to control a BMI.

In this study, we systematically investigated for the first time the extent to which flexion and extension movements involving the fingers, wrist, and elbow could be classified from ECoG signals recorded from sensorimotor cortex at varying spatial scales. We found that power in the high-gamma (HG) band (70–110 Hz) of these ECoG signals provided enough information to classify the different movements using a linear classifier, with more movements being distinguishable at the macro-ECoG and HD-ECoG scales than at the micro-ECoG scale. These results suggest that neural representations of movements about these joints may be separable enough when using ECoG electrodes spread over wider cortical areas to provide BMI users control over individual DoFs. An ECoG-based model of flexion and extension holds potential to provide practical prosthesis control as an alternative to more invasive penetrating electrodes.

II. METHODS

A. Subject Info

The participants ($N = 4$) in this study were implanted with surface ECoG electrode grids and strips to localize their respective seizure onset zones and guide surgical treatment for drug-resistant epilepsy. Table I details patient demographics and implant locations. All subjects gave informed consent for testing according to a protocol approved by the Institutional Review Board of the Johns Hopkins Medical Institutions.

B. Data Collection

ECoG electrodes were implanted for a period of 7–14 days during which the patients performed experimental testing. Electrode grids included macro-ECoG arrays (2.3 mm exposed diameter, 10 mm spacing; Adtech, Racine, WI or PMT Corp., Chanhassen, MN), high-density (HD) ECoG arrays (2 mm diameter, 5 mm spacing; PMT Corp.), and micro-ECoG arrays (75 μ m diameter, 0.9 mm spacing; PMT Corp.). To display electrode locations with respect to cortical surface anatomy, a pre-surgical MRI was volumetrically co-registered with a post-implant CT using BioImage Suite [23]. Figure 1 shows each patient's electrode implants and specifies the electrode grid(s) selected for analyses. These electrode grids were chosen because they covered the largest portion of the sensorimotor cortical surface, which was the target implant location most relevant to our movement paradigm. ECoG signals were recorded at 1 kHz using a Blackrock Neuroport system or 2 kHz using a Nihon Kohden system (Table I).

C. Task Description

Subjects were visually cued with images to flex or extend: (1) all their fingers simultaneously, (2) their hand about the wrist, or (3) their forearm about the elbow. These motions will be referred to as finger flexion and extension, wrist flexion and extension, and elbow flexion and extension. All movements were made with the arm contralateral to the implanted grid while keeping the other arm still (Figure S1). Each trial began with a

centered crosshair displayed for 3–4 s, followed by the visual cue displayed for 2 s. For patient P1, the visual cue was followed by a blank screen for 0.5–1.5 s, and then followed by the word Go to cue the subject to initiate the movement. The task was later shortened by removing the Go cue and preceding blank screen to avoid eliciting neural activity associated with anticipation and possible suppression of movements before the Go cue. Patients P2–P4 were thus instructed to initiate the movement as soon as the visual cue was displayed. In total, these movements comprised 6 different movements to be classified (although shoulder abduction and adduction were originally included, patient P3 often mistakenly performed elbow movements when cued for shoulder movements, so we excluded shoulder movements from subsequent analyses for all patients). Subjects were instructed to start each trial with their arm in a neutral rest position, which would allow full range of flexion and extension about the different joints, and to return to this rest position after performing the visually cued movement. Table I indicates which joints the subjects were required to move and the number of trials performed.

D. Neural Data Processing

Electrodes were excluded from further analyses if their recorded signal included artifacts or epileptiform activity, as determined by manual inspection. ECoG signals from the electrodes selected for analysis were spatially re-referenced by subtracting the common average signal of all the selected electrodes. To establish a baseline period, signals were segmented from 500 ms before the visual cue to the onset of the visual cue of each trial. Each trial's response period was segmented as a 5 s period after cue onset. High-gamma (HG, 70–110 Hz) power was extracted by taking the power spectral density of these segmented signals, within bins of 256 ms shifted by 8 ms, and summing the power of all frequencies between 70 and 110 Hz (2 Hz bins) at each time bin. The logarithm (base 10) of HG power in each trial's response period was then normalized (Z-score computation) to the combined baseline periods of all trials. Task-related power increases above HG (> 110 Hz) were excluded when computing the band power as later analyses showed that higher frequencies offered no increase in classification power, likely due to redundant information (data not shown). Though task-related power decreases were observed in alpha and beta frequencies, we excluded them from our analyses as decoding from these features resulted in much lower classification accuracies than decoding from HG features.

E. Movement Data Processing

Upper limb muscle activity in each patient was also recorded as electromyogram (EMG) signals at the same frequency as ECoG signals. Bipolar and monopolar surface EMG electrodes were placed on the belly of the most superficial flexor and extensor muscles responsible for movement at each joint (Table I). Signals were notch filtered at 60 Hz and its harmonics (120, 180, 240, 300, 360, 420, and 480 Hz) to remove power line noise, and high pass filtered at 20 Hz to remove low frequency artifacts. Signals were then rectified by taking the absolute value and segmented as described in Section II-D. Each trial's response period was normalized to its respective baseline period (Z-score computation). Movement onset was visually marked for each trial as the earliest time showing an increase in signal amplitude in the monopolar electrodes or bipolar pairs most relevant to movement about the respective joint. Additionally, movement offset time was determined from the trial-averaged

EMG signal recorded from electrode(s) most proximal to the respective joint for each movement.

The HG power trials were then aligned to movement onset and re-segmented such that all trials shared the same pre- and post-movement onset periods. Each patient's data was segmented differently to accommodate the shortest lag until movement onset, as well as the shortest period before trial completion across all trials.

F. Movement Decoding

The six movements shown in Figure S1 were classified using HG power in the electrodes selected for analysis in each patient. Patient P3 had both a macro-ECoG array and two micro-ECoG arrays placed on sensorimotor cortex, and the decoding analysis described below was performed with each array separately.

Electrodes that showed a significant difference between trial-averaged HG power (HG power at each time point averaged across a set of trials) of different movements (ANOVA, $p < 0.05$) during at least 5% of the time points within the trial period were selected for decoding. Offline decoding was assessed as a function of time, with respect to movement onset, using a decoding window size comparable to that used by a recent ECoG study investigating offline decoding of arm movement kinematic parameters (300 ms window shifted by 50 ms) [13]. Due to the specific window length and overlap parameters used during spectral estimation (Section II-D), the sliding window we used to compute a time-dependent accuracy curve was 328 ms shifted by 40 ms. The accuracy at each time point was aligned to the lagging edge of the sliding window. This time-dependent accuracy curve showed the latency relative to movement onset of when neural representations of different movements were most discriminable.

Within each sliding window, trials were partitioned to train a decoding model through linear discriminant analysis (LDA), as used in previous ECoG decoding studies [12,24], and to test this model's accuracy through 10-fold cross validation. The features used to train this model consisted of each trial's average HG power from the decoding electrodes. To assess whether the resulting accuracy was significantly higher than chance ($p < 0.05$, FDR-corrected), a null probability distribution was generated by randomly shuffling the movement labels and performing classification (as previously described) 1,000 times. P-values were generated non-parametrically by calculating the percentage of random shuffles producing classification accuracies higher than the observed classification accuracy within the sliding window.

Confusion matrices were constructed offline to show the decoding power of time-averaged (average HG power of a trial within a period of time) ECoG signals within a specific time window, henceforth referred to as the "bounded time window", which was longer than the sliding window described above (window length ranged between 0.87–1.89 s across patients). Averaging neural signals within a longer period of the movement duration provided more discriminability between movements by improving the signal to noise ratio. Because trials included data from both cued movements and return movements back to the rest position, the limits of this time window were chosen such that the classification analysis was representative of only the cued movements. The window began where the time-

dependent accuracy curve became significantly higher than chance, thus excluding the period that showed no discriminatory power. The window ended at the time of the earliest occurring cued movement offset (across all movements), which prevented classification to be skewed by neural activity corresponding to the movement back to the rest position. Electrodes that showed a significant difference between each movement's trial-averaged HG power across the entire bounded time window (ANOVA, $p < 0.05$) were re-selected for decoding. LDA was used to train and test a 6-class model (all 6 flexion and extension movements) with the corresponding features computed as previously explained. This method was also used to train and test a 3-class model that classified the joint involved in the movement during each trial, where flexion and extension trials for each joint were grouped together (combined fingers vs. combined wrist vs. combined elbow movements), and a 2-class (flexion vs. extension) model for each joint separately.

G. Characterizing Cortical Contributions to Decoding

To visualize the decoding contribution of each recording site to movement classification within the bounded time window, the vector weights from the linear model were analyzed. The linear model for multi-class discrimination analysis resulted in a weight vector for each electrode. The magnitude of each electrode's weight vector was computed and normalized to the highest magnitude across all electrodes (Figure 1).

To further explore the movement-specific HG activation in each electrode, the log-transformed and normalized HG power (see Section II-D) was averaged across all the trials for each movement, and across the bounded time window. A brain map for each patient displaying this average HG power at each electrode selected for analysis was created for each of the six movements.

To investigate differences between neural representations of movements about the same joint, we compared the time-averaged HG power changes across all electrodes during the respective flexion and extension trials. The time-averaged HG powers were used to determine if activity at each electrode was significantly different between flexion and extension (two-tailed t-test, $p < 0.05$, FDR-corrected). For each joint, we calculated the percentage of electrodes showing significantly different HG activity between flexion and extension within the group of significantly active electrodes (with respect to baseline) for either movement.

III. RESULTS

A. Movement-related Cortical Activation

We computed time-frequency plots showing the average neural activity for each movement and single-trial raster plots showing HG power changes in each trial for each electrode to confirm significant neural activity in the HG band (Figures S2 and S3). Task-related cortical activation occurred in spatial and temporal patterns consistent with the known functional anatomy of hand and arm movements as described in previous studies [25].

B. Time-dependent Classification Performance

A movement-aligned time-dependent accuracy curve was created for each subject (Figure 2) to show the classification accuracy of the 6-class model (chance 16.7%, calculated non-parametrically) across the duration of a movement trial. Using a 328 ms sliding window, we observed that accuracy peaked at 56%, 59%, 68%, and 49% for patients P1-P4 respectively (at roughly around 0.4 s after movement onset for patients P1-P3 and at movement onset for P4), and then slowly fell. Decoding accuracy began to steadily increase as early as 0.5 s before movement onset in patient P4.

C. Classification Accuracies within a Time-Bounded Window

To reduce noise in our decoding model, time-averaged neural signals were classified within a bounded time window (see Section II-F), which included a larger time interval than the sliding window used above to compute performance across time. Confusion matrices were created for each patient to show how well each movement was classified (Figure 3A-D). Classification of the six movements yielded accuracies of 67.9%, 61.7%, 82.8%, and 63.8% ($p < 0.05$, chance 16.7%, calculated non-parametrically) for patients P1-P4, respectively. While finger flexion was generally more accurately classified than the other movements across all subjects, followed by finger extension in three of the four subjects, the other joint movements had varied decoding accuracies across the four subjects. In general, there seemed to be no systematic confusion between the six movement classes across all subjects.

To further elucidate the discriminatory power along individual joints (fingers, wrist, and elbow), the time averaged neural signals were again classified using a 3-class model within the same bounded time window (Figure 3E). Classification about the three joint classes yielded accuracies of 69%, 68%, 90%, and 73% ($p < 0.05$, chance 33.3%) for patients P1-P4, respectively. Although elbow flexion and extension individually yielded relatively low classification accuracies in patients P1 and P2, combined elbow movements (flexion or extension) were classified with 88% and 80% accuracy in patients P1 and P2, respectively. This was likely due to lower HG activity observed during elbow movements than during finger and wrist movements. The accuracy of classifying combined elbow movements from patient P3 was higher than correctly classifying elbow flexion or extension individually (94% compared to 81% and 73% for flexion and extension, respectively). However, combined finger and combined wrist movement classification accuracies were consistent with those for flexion and extension individually. Similarly, the joint classification accuracies from patient P4 were also consistent with those of individual flexion and extension movements. Moreover, classifying flexion vs. extension for each joint separately yielded higher accuracies (Figure 3F; $p < 0.05$, chance 50%) than those obtained by classifying all flexion and extension movements together, with the exception of finger movements in patient P2 and of elbow movements in patients P1 and P4.

D. Cortical Areas Contributing to Decoding

Decoding contributions were calculated using the weight vectors of each electrode to assess which electrodes offered the most classification power in discriminating between the 6 movements (Figure 1). In patient P1, electrodes in the posterior corner of the HD grid showed high discriminatory power, along with one weakly contributing anterior electrode

(Figure 1A). It was likely that the area with ictal activity contributed less to decoding because it was generally outside of the upper limb representations in primary motor (M1) and somatosensory (S1) cortices. In patients P2, P3 (macrogrids), and P4 (HD-grid), dorsal electrodes contributed most to decoding, likely because these electrodes covered upper limb representations in M1 and S1 and resulted in greater differences in HG activity elicited by different movements (Figures 1B, 1C, 1D, 4D, 4G and 4H).

We also compared the neural representation of movements about individual joints based on their respective HG activations (Figure 4). Elbow movement showed the most widespread activation in patients P3 and P4 (Figures 4G and 4H), while the relatively lateral grid placement (i.e., compared to expected areas with upper arm representations) may have prevented such observations in patients P1 and P2. Rather, electrodes in the top right corner of the HD grid showed higher activity for finger and wrist movements in patient P1 (Figure 4C). Similarly, finger movements and wrist flexion showed higher HG activity in the more dorsal electrodes of the grid implanted in patient P2 (Figure 4D). In patient P4, most of the active electrodes were confined to the group of electrodes within and near the hand knob of M1, with a few weakly active electrodes along S1 as well (Figure 4H). The limited coverage of HD-ECoG electrodes in the hand area of M1 and the presence of a lesion occupying the posterior half of the hand area of S1 may have resulted in the limited activity observed during these movements.

In patients P1-P3, the percentage of electrodes whose activity significantly differed between flexion and extension was generally very high for finger movements and low for movements about the elbow. This could have been due to a larger area in sensorimotor cortex devoted to discriminating between neural representations of flexion and extension of the fingers rather than those of the elbow [26]. Additionally, compared to patients P3 and P4, patients P1 and P2 had high proportions of electrodes showing significantly different HG activity between wrist flexion and extension, which contributed highly to decoding of wrist movements, likely due to the lateral placement of electrode grids. Furthermore, across all joints of each patient, most electrodes typically showed higher HG power for flexion than for extension. It should be noted that the HG powers displayed on the brain maps only include electrodes with significant HG activity (relative to baseline) during flexion and/or extension. There were additional electrodes which showed significant differences between flexion and extension, but were not displayed on the brain maps since the HG activity in those electrodes were not significantly different from baseline for neither flexion nor extension.

E. Classification Accuracies at the Micro-ECoG scale

As patient P3 was implanted with macro- and micro-ECoG arrays in the sensorimotor cortex, we compared the movement classification accuracy across different spatial scales. The classification accuracies obtained for the 6-class model (chance 16.7%, calculated non-parametrically) using the bounded time window were 30.6% and 43.9% ($p < 0.05$) for the anterior (AMIC) and posterior (PMIC) micro-ECoG arrays, respectively. Figure 5 shows that elbow flexion was most accurately classified (67%) using AMIC, and finger flexion was the most accurately classified (62%) using PMIC. The classification accuracies ranged from 11% to 46% for all other movements.

Maps showing the average HG power changes at each electrode also showed different patterns of activity between the six movements (Figure S4). Electrodes in PMIC showed higher HG power changes than AMIC electrodes for all movements, with finger flexion and extension showing the highest activity, followed by the wrist and then elbow movements. Additionally, there were many electrodes in PMIC which showed significantly different activity between finger flexion and extension. Electrodes in AMIC showed very low HG power changes during finger and wrist movements, but showed higher HG power changes for elbow flexion and extension.

IV. DISCUSSION

A. Overall Decoding Performance

Previous studies have approached decoding of movement about multiple joints through various methods. Fifer et al. [12] showed that ECoG can be used to discriminate two movements (reach and grasp) involving simultaneous control of multiple joints along the upper limb. Another group, using ECoG signals from sensorimotor cortex of a tetraplegic patient, decoded movements about individual joints for directional cursor control, rather than control of a robotic arm [11]. While the subject was instructed to attempt repetitive thumb, wrist, and elbow flexion and extension movements to control a cursor in a 3D cartesian coordinate space, the authors did not focus on differentiating the neural representations of flexion and extension movements. Additionally, Yanagisawa et al. [22] showed preliminary evidence that ECoG signals in patients with varying degrees of motor dysfunction can be used to decode upper limb flexion and extension movements of the elbow and fingers. The authors then used joint-specific decoders to provide users real-time control of a prosthetic arm.

More recently, Wang et al. [27] decoded movements about individual joints of the upper limb to investigate differences in classification power between standard and HD ECoG electrode coverage. While the authors decoded wrist, elbow, shoulder, and finger movements, they did not decode flexion and extension movements separately. Further, Jiang et al. [21] studied the neural representations of finger flexion and extension movements in the hand area of sensorimotor cortex and suggested that HD-ECoG recordings could be used to classify flexion and extension of all the fingers together. In this study, we expanded on the previous research by investigating the degree to which ECoG recordings at different spatial scales (1-mm, 5-mm, and 10-mm spacing) can be used to discriminate flexion and extension at both proximal and distal joints along the upper limb.

Wang et al. [28] investigated the neural activation profiles in primary motor cortex as subjects performed flexion and extension movements individually at various speeds and durations. The authors found that HG power remained elevated throughout each movement, suggesting there was continuous HG power modulation throughout the movement rather than only transient HG responses. Accordingly, we computed time-dependent classification curves to show the average decoding accuracy over the entire duration of each trial, which included both the cued flexion or extension, as well as a return motion back to the rest position. To avoid including both initial and return movements during classification of our time-averaged signals (see Section II-F), we decoded from a bounded time window (which

included the cued movement and excluded the return movement), and achieved accuracies of 68%, 62%, 83%, and 64% for patients P1-P4, respectively. By leveraging the differences between movement-specific HG power modulations across the entirety of an individual movement, we achieved higher classification accuracy than when using short time windows to compute the time-dependent classification curves. This suggests that the neural representations of upper limb flexion and extension movements are more discriminable across their entire duration than at a single time point during movement execution. Additional discriminatory power from longer duration movements (i.e. elbow flexion and extension) could have been excluded as the electrode signals were curtailed by the bounded time window, which was fit to the movement with the shortest time period as determined from EMG signals. Also, decoding of shorter duration movements (i.e. finger flexion and extension) could have been negatively impacted by preparatory neural activity toward the end of the bounded time window associated with the return movement. However, to properly account for this activity, the duration of preparatory activity would have to be known, which is not trivial to estimate.

Our results provide evidence for possible strategies which use different decoding durations to control individual joints of an upper limb prosthetic. Pre-movement and perimovement onset decoding (seen as early as 0.5 s in patient P4, Figure 2) may allow a BMI user to trigger a specific movement, while longer time intervals may be more useful in decoding the desired movement to completion. Additionally, we observed that classification accuracies between flexion and extension of the same joint were generally higher if the joint was already specified (Figure 3F). This suggests that decoding the joint first followed by the type of joint movement could lead to more accurate classification of these upper limb movements. These decoding results have considerable applicability to upper limb BMI, where classification of multiple joint flexion and extension would facilitate whole limb prosthesis control.

B. Representation of Flexion and Extension at Individual Joints

Differences in grid positions on the medial-lateral axis may have contributed to the variance in classification accuracies across subjects. The wide sensorimotor coverage seen in patient P3 could have captured the most complete neural representations of upper limb movements, in turn yielding the highest classification accuracies. In contrast, the smaller and more lateral coverages seen in patients P1 and P2 may not have encompassed enough of the upper limb representations in sensorimotor cortex to decode both forearm and upper arm movements as accurately, resulting in lower overall classification accuracies. Similarly, the HD-ECOG electrodes in patient P4 may not have covered all relevant upper limb cortical regions. Additionally, upper limb representations within the sensorimotor cortex of this subject could have been remapped due to a lesion along the postcentral gyrus. These factors could have contributed to lower classification accuracies than those observed in other subjects.

We observed that finger flexion was classified more accurately than the other movements in patients P1-P3. Since the decoding models for these patients included electrodes from both motor and sensory cortices, sensory feedback received during the movements may have contributed additional discriminatory power, especially during finger flexion as the fingers

come in contact with the palm. The high classification accuracy for finger extension in patients P1 and P3 may have similarly been influenced by sensory feedback, perhaps from the stretch response of mechanoreceptors in the hand. While finger flexion and extension were also classified fairly well in patient P4, they were not as accurately classified, likely due to the limited coverage of hand motor representations on precentral gyrus and remapping of hand sensory representations due to a lesion on the postcentral gyrus.

The degree of similarity between neural representations of movements about the same joint likely influenced those movements' classification accuracies as well. Misclassification between flexion and extension about the same joint could be explained by similar HG activations among electrodes between those movements, as seen for elbow movements in patients P1 and P2 and for elbow and wrist movements in patient P3 (Figure 4). These similar HG activations also likely caused the lower performance observed across all movements in patient P4. A large difference in HG activations between flexion and extension of the same joint could have explained higher within-joint classification rates, such as those seen for finger movements in patients P1 and P3. However, this was not the case for wrist movements in patient P1 and for finger and wrist movements in patient P2. Despite observing differences in average HG activity between flexion and extension movements, a high misclassification within finger and wrist movements could have been caused by a high variance within each electrode's behavior.

In general, a greater proportion of electrodes showed significant differences between finger flexion and extension than between elbow flexion and extension. Hand movements involve more degrees of freedom than elbow movements, so it may be possible that distinguishing between different hand movements requires more neural populations within sensorimotor cortex than distinguishing between different movements about the elbow. Furthermore, even though elbow flexion and extension were very discriminable from other joint movements, discrimination between elbow flexion and extension was lower due to the small percentage of electrodes showing significant differences in HG activity (especially in patients P1, P2, and P4). Among the electrodes that did show differences in HG activations between flexion and extension at the same joint, we observed that most of these electrodes showed higher HG power for flexion compared to extension. It may be possible that, in general, flexion about a joint elicits greater muscle activity than extension, which could translate into higher HG power within the respective neural populations.

C. Organization of Individual Joint Representations in Sensorimotor Cortex

Early cortical stimulation studies by Penfield and Boldrey suggested that representations of the upper arm, forearm, and hand are organized somatotopically in a medial to lateral fashion on both the precentral and postcentral gyri [26]. Microelectrode recordings in NHPs have confirmed this somatotopic model in the primary somatosensory cortex (S1) by demonstrating a medial to lateral organization of arm, wrist, hand, and finger regions within a complete body map [29–32]. Recent fMRI and intracortical microstimulation (ICMS) studies in humans have also provided evidence of a somatotopic representation in S1, although they focused mainly on the organization of finger representations [33–35].

In the primary motor cortex (M1), however, later fMRI, ECoG, and cortical stimulation studies have not observed such clear somatotopic organizations. Using fMRI, Klein-schmidt et al. [36] showed overlapping somatotopy between representations of various wrist, hand, and individual finger movements within the hand area of M1. Lotze et al. [37] similarly showed overlapping activation maxima of upper limb movements using conventional fMRI 3D-evaluation, but also, showed distinct activation maxima using a 2D-projection method. Moreover, Alkadhi et al. [38] showed significantly different volumetric centers of gravity (COGs) during upper limb movements despite substantial somatotopic overlap. Using ECoG recordings from human sensorimotor cortex, Miller et al. [39] reported that motor-related low frequency power was more spatially distributed during various limb movements, but that high frequency power (76–100 Hz) was not rigidly somatotopically organized. Furthermore, by stimulating various muscle-specific sites in M1 of NHPs, several groups have suggested that neural representations of different forelimb regions interleave and overlap to a higher degree than proposed by early somatotopy studies [40–43]. One particular group has shown that ICMS delivered at individual sites along M1 evoked complex, multi-joint movements rather than movements about a single joint [44,45]. Rather than a somatotopic map of individual joint representations, the authors suggested that the organization of M1 may be based on a spatial map of complex actions.

In our study, we observed HG power activation patterns that suggest a medial to lateral organization of neural representations of movements about the elbow, wrist, and of the fingers on the sensorimotor cortex (patients P2 and P3). Generally, this organization was more pronounced on the postcentral gyrus than on the precentral gyrus. While we also observed widespread activity in lateral electrodes for elbow movements in patient P3, this activity could have arisen from tactile feedback in the forearm and hand, which were in contact with the surface supporting the arm. This could have obscured the underlying somatotopic organization of joints on the postcentral gyrus suggested by previous S1 studies. On the precentral gyrus of patient P3, we observed that electrodes active for different joints were not necessarily localized to different areas of motor cortex, and a subset of electrodes was also active during multiple movements about different joints. These observations are comparable to previous M1 studies suggesting cortical representations of individual joints are scattered and overlapping.

D. Classification of Movements at Micro-ECoG Scale

Since each flexion or extension movement likely involved activations within larger or more scattered neural populations than were sampled by a single micro-ECoG array, recording from a wider area of cortex may be needed to adequately classify different joint movements. However, micro-ECoG electrodes within a single array were able to show varied HG differences between flexion and extension about a specific joint. Therefore, even though a macro-ECoG electrode may show significant activity for a specific movement, the neural population within that recording area may not be uniformly active during that movement. This suggests that the higher spatial resolution of a micro-ECoG array may potentially provide more discriminable information of neural representations from different joint movements on a smaller scale within the sensorimotor cortex. If micro-ECoG arrays could be accurately placed in a cortical area with movement-specific activation, this higher

resolution activity may improve decoding performance from these arrays. Furthermore, a decoder built from micro- and macro-ECoG signals may be used to both classify individual joint movements and provide additional discrimination of finer movements about those joints (e.g. different finger movements).

While higher decoding accuracy might have been possible with more precise micro-ECoG placement or coverage of a wider cortical area by multiple micro-ECoG arrays, this would not have been feasible given the clinical circumstances. Furthermore, our statistical method of selecting channels for decoding required that these channels show significant differences between trial-averaged HG signals of at least two movements. However, some electrodes may have only minimally passed these criteria, while still showing a high variance across neural signals of different movements, resulting in our model's suboptimal performance. Finally, as only one patient had micro-ECoG recordings, it is difficult to infer whether micro-scale neural representations from similar cortical regions in the other subjects would have shown higher decoding power.

E. Significance and Future Work

Although the decoding architecture we used for this offline analysis is probably not ideal for online implementation, our results do support ECoG as a recording modality from which native neural representations of upper limb movements can be decoded. Moreover, future ECoG-based online decoders modelled on these native neural representations may not require extensive user-training periods (like those required by MEA-based models) to achieve adequate control of these individual degrees of freedom. Any additional training could be used to refine the performance of the BMI and compensate for any reorganization that might have taken place due to an injury that resulted in loss of output from motor cortex.

We have shown that flexion and extension of upper limb joints could involve varying degrees of activity from widespread regions of the sensorimotor cortex. This was shown best by the macro-ECoG grid in patient P3, whose coverage captured widespread activity and likely led to high decoding across joints (Figures 3C and 3E). While HD-ECoG arrays could have resulted in higher accuracies, their suboptimal cortical coverage likely contributed to a decreased classification performance in patients P1 and P4. However, we propose that orienting an HD-ECoG electrode array along the length of the sensorimotor cortex could lead to improved discriminatory power as a result of sampling widespread neural activation at an even higher spatial resolution than that of the macro-ECoG array (as shown in [27]).

It is worth mentioning that we observed that electrodes in the postcentral gyrus contributed the most to decoding (Figure 1), suggesting that sensory feedback may be providing more discriminable information about these movements than the motor cortex output. While patients who would benefit from BMI would likely have significantly altered or reduced somatosensory input, neural representations of imagined or attempted flexion and extension movements could offer enough discriminable activity to be decodable through an ECoG-based BMI [11,22]. Furthermore, though lower than post-movement onset decoding accuracies, patient P4 also showed pre-movement onset decoding accuracies significantly above chance (Figure 2), suggesting that there is discriminable neural activation prior to

movement execution. This pre-movement activity could be further explored with a chronic ECoG implant in patients with upper limb paralysis.

Though several groups have successfully decoded neural activity in the context of 3D center-out reaching tasks [1,2,13], the limitation to this approach is that limb control is directed to targets in an egocentric reference frame. The additional control provided by decoding flexion and extension of individual upper limb joints could potentially accommodate movements in object-centered reference frames, as suggested by Nakanishi et al., who showed that 3D joint trajectories can be predicted from ECoG signals recorded during a object transfer task [16]. Further, decoding individual joint flexion and extension may facilitate simple corrective movements requiring only one degree of freedom, like reaching for an object at a wider elbow angle than originally planned. Further work will be needed, however, to achieve continuous decoding of joint angles for flexion and extension at individual joints.

An ECoG-based BMI with online classification of independent flexion and extension movements at different joints could potentially be used to restore intuitive motor function in patients with upper limb amputations through robotic prosthetics, or in patients with upper limb paralysis through functional electrical stimulation (FES) or control of an exoskeleton. However, though FES has been well responsive to single and multijoint decoded inputs from MEAs [46], further improvements in decoding performance may be realized through methods such as hierarchical linear classifiers, which first classify movement vs. rest and then classify among different possible movements [24]. Furthermore, a two-step decoder that combines classification steps (movement vs. rest, movement vs. movement), and a regression step (movement trajectory), as in [13], could potentially provide additional benefits. With these methods, providing control of reach and grasp movements as achieved in previous studies with additional control of individual joint movements could potentially broaden the spectrum of activities achievable by BMI users.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure. 1.

Brain map reconstructions for patients P1, P2, P3, and P4 (A, B, C, and D, respectively).

Blue rectangles surround the ECoG electrodes that were selected for analyses in each patient. For patient P3, two micro-ECoG arrays (circled in blue) located on the sensorimotor cortex were also used for analyses. The central sulcus is outlined in black. Post-experimental analysis showed that patient P1 displayed significant ictal activity at electrode sites marked by beige-colored shapes. Therefore, during common average referencing, ECoG signals from electrodes within the green dotted box were spatially referenced separately from the other electrodes within the solid blue box. Electrodes are marked with colors on the yellow-red spectrum to represent their contribution to classifying the 6 movements, where the decoding weights of electrodes are normalized to a scale from 0 to 1. Smaller (yellow) electrodes contributed little to decoding, while large (dark red) electrodes contributed most to decoding.

Figure. 2.

Plots showing accuracy of classifying 6 movements as a function of time, for patients P1, P2, P3, and P4 (A, B, C, and D, respectively). The blue trace represents average time-dependent classification accuracy after 10-fold cross validation, and the black horizontal trace represents average chance accuracy (1,000 shuffles) with respect to movement onset (black vertical line). The blue shading represents the standard deviation of the classification accuracies across the 10 folds. The red shaded regions represent where the decoding accuracy was significantly higher than chance ($p < 0.05$, FDR-corrected).

Figure. 3.

Confusion matrices are shown for patients P1, P2, P3, and P4 (A, B, C, and D, respectively). Classification accuracies were computed within a window of -0.12 to 0.9 s, -0.22 to 0.65 s, -0.18 to 1.15 s, and -0.54 to 1.25 s relative to movement onset for patients P1-P4, respectively. Abbreviations F Flx, F Ext, W Flx, W Ext, E Flx, and E Ext represent finger, wrist, and elbow flexion and extension. The labels on the vertical axis represent the visually cued (actual) movements, and the labels on the horizontal axis represent the movements predicted by the classifier. Dark blue to light green and yellow to dark red displays low to

middle to high classification accuracy (0–1). Confusion matrices for joint classification are also shown for patients P1-P4 (E), in which flexion and extension trials for each joint were grouped together. Finally, accuracies for flexion vs. extension at each joint separately are included in a table (F).

Figure. 4.

Log-transformed HG power changes were only analyzed for the electrodes outlined by red boxes in A, B, E, and F for patients P1-P4. The central sulcus is outlined in black. C, D, G, and H display brain maps showing the movement-specific average of log-transformed HG power changes within the respective bounded time windows in those electrodes. The color and size of the electrodes were varied to illustrate significant log-transformed power changes (relative to baseline), with units of $\log_{10}(V^2/Hz)$. Green, blue, and yellow circles highlight the subset of electrodes that showed significantly different HG activity between flexion and extension of fingers, wrist, and elbow, respectively. Percentages of significantly active electrodes showing a significant difference between flexion and extension about a specific joint are displayed between the flexion and extension brain maps. Cyan triangles mark those electrodes that showed higher gamma power for flexion or extension of each joint. Beige

shapes surrounding electrodes on the brain map of patient P1 (A) represent electrodes with high ictal and interictal activity.

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Figure. 5. A and B show the decoding contributions of the electrodes in PMIC and AMIC, respectively, used to classify the six movements. Electrodes are marked with colors on the yellow-red spectrum to represent their contribution to movement classification. Smaller (yellow) electrodes contributed little to decoding, while large (dark red) electrodes contributed most to decoding. Classification accuracy from PMIC electrodes was computed from a window between -0.144 s to 1.15 s relative to movement onset, and the accuracy from AMIC electrodes was computed from a window between 0.056 s to 1.15 s post-movement onset. The central sulcus is outlined in black. C and D show the confusion matrices resulting from classification models using PMIC and AMIC arrays, respectively. Abbreviations F Flx, F Ext, W Flx, W Ext, E Flx, and E Ext represent fingers, wrist, and elbow flexion and extension.

TABLE I.
PATIENT DEMOGRAPHICS, IMPLANT LOCATIONS, NEURAL AND MUSCLE
RECORDING DETAILS

PFG and RFG are abbreviations for posterior frontal and right frontal grids (4×5 and 8×8 macro-ECOG arrays, respectively), while FPG and HDG are abbreviations for fronto-parietal grid and high-density grid (8×16 high density arrays). AMIC and PMIC are abbreviations for anterior and posterior micro-ECOG electrodes (4×4 arrays). Abbreviations EDC, FDS, BB, TB, AD, and PD are extensor digitorum communis, flexor digitorum superficialis, biceps brachii, triceps brachii, anterior deltoid, and posterior deltoid muscles, respectively.

Patient	Gender	Age (years)	Implant hemisphere/ Grid name	Software/ Sampling frequency	Electrode polarity/ Recorded muscles	Total Trials/ Trials per movement
P1	M	27	Left; FPG (subdural)	Blackrock (1 kHz)	Bipolar: EDC, FDS	234; 39
P2	F	36	Left; PFG (epidural)	Nihon Kohden (2 kHz)	Bipolar: EDC, FDS, BB, TB	240; 40
P3	M	22	Right; RFG, AMIC, PMIC (subdural)	Blackrock (1 kHz)	Bipolar: EDC, FDS Monopolar: BB, TB, AD, PD	156; 26
P4	M	18	Right; HDG, RFG (subdural)	Blackrock (1 kHz)	Bipolar: EDC, FDS, BB, TB, AD, PD	204; 34