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Functional MRI-based identification of brain areas involved in motor imagery for implantable brain–computer interfaces

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Abstract

For the development of minimally invasive brain–computer interfaces (BCIs), it is important to accurately localize the area of implantation. Using fMRI, we investigated which brain areas are involved in motor imagery. Twelve healthy subjects performed a motor execution and imagery task during separate fMRI and EEG measurements. fMRI results showed that during imagery, premotor and parietal areas were most robustly activated in individual subjects, but surprisingly, no activation was found in the primary motor cortex. EEG results showed that spectral power decreases in contralateral sensorimotor rhythms (8–24 Hz) during both movement and imagery. To further verify the involvement of the motor imagery areas found with fMRI, one epilepsy patient performed the same task during both fMRI and ECoG recordings. Significant ECoG low (8–24 Hz) and high (65–95 Hz) frequency power changes were observed selectively on premotor cortex and these co-localized with fMRI. During a subsequent BCI task, excellent performance (91%) was obtained based on ECoG power changes from the localized premotor area. These results indicate that other areas than the primary motor area may be more reliably activated during motor imagery. Specifically, the premotor cortex may be a better area to implant an invasive BCI.

1. Introduction

Implantable brain–computer interfaces (BCIs) require a stable, reliable signal from an area that can easily be localized before implanting a device [1]. Motor imagery is one of the most used strategies to control a non-invasive BCI, and this study investigates whether we can localize a brain area that is specifically and reliably activated during motor imagery.

BCI studies recording multiunits from several areas in the macaque have shown that in addition to primary motor cortex

(M1), premotor cortex (PMc) and supplementary motor areas (SMA) have signals that would perform just as well to control a BCI [2]. In humans, functional magnetic resonance imaging (fMRI) allows us to measure the whole brain non-invasively with high spatial resolution and to investigate which areas are activated during motor imagery. Previous fMRI studies have shown that group analyses reveal largely consistent PMc, SMA and dorsal parietal cortex activation during motor imagery [3–11]. In contrast, highly variable results in M1 activation during motor imagery have been observed. For reviews, see [9, 11]. Most of these studies have been performed on a group level, but implanting a BCI in a patient requires localization in

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an individual subject. As the areas active during motor imagery can differ between subjects with different motor imagery ability [10] and activity patterns can change with practice [12, 13], it is important to know which of these motor imagery areas can be identified on a single subject basis. We have previously shown that fMRI can accurately localize function-specific regions in individuals [1, 14]. Here, we investigate which brain areas are most robustly activated during motor imagery as it is used in a BCI setup.

We recorded fMRI and EEG separately in 12 subjects and found that in fMRI, premotor areas were robustly activated during imagery in every individual subject. ECoG recordings in one patient showed that on these premotor areas spectral power changes co-localized with preoperative fMRI results in the same subject. Furthermore, using the signal from this premotor area during a BCI resulted in very good performance (91%).

2. Methods

2.1. Subjects

Twelve healthy right-handed BCI naïve participants (age range 19–25 years, 6 females) and one patient (age 17, female) scheduled for the implantation of ECoG arrays (AdTech, Racine, WI, USA) for epilepsy monitoring gave written informed consent to participate in this study. This study was approved by the ethical committee of the University Medical Center Utrecht, in accordance with the Declaration of Helsinki 2008.

2.2. Task

All subjects performed a motor execution and imagery task. The task consisted of an instruction ('move', 'imagine' or 'rest', presented for 1.3 s) followed by a block of 15.7 s during which a square flashed every 600 ms interleaved by a fixation cross. The subjects were instructed to respectively execute or kinesthetically imagine tapping an alternating finger of the right hand to the thumb at the rhythm of the square or think of nothing in particular during the rest condition. The patient performed the same task but with the left hand.

2.3. fMRI measurement

Scans were acquired on a Philips 3T Achieva. During the motor imagery task, 871 fMRI PRESTO scans [15] were acquired ($FA = 10$ degrees, $FOV = 224 \times 256 \times 160$ mm, voxel size $4 \times 4 \times 4$ mm, $TE/TR = 33/23$ ms, time per whole-brain volume 0.6 s). Functional scans were realigned and coregistered to an anatomical scan ($FA = 8$ degrees, $FOV = 288 \times 288 \times 175$, voxel size $1 \times 1 \times 1$ mm, $TE/TR = 3.8/8.4$ ms). Data from the healthy subjects were normalized to MNI space using a unified segmentation procedure [16] and smoothed with an 8 mm full width half max to allow group comparisons. EMG was measured over the right hand extensor digitorum communis and abductor pollicis brevis with four scanner compatible surface electrodes (MR Physiology Logging, Philips Medical Systems Nederland

B.V., Eindhoven, The Netherlands). The EMG data were analyzed similarly, as described in [17]. First, the EMG signal was notch filtered at 45 and 90 Hz to remove fMRI artifacts, and high pass filtered at 10 Hz to remove movement artifacts. To regain low frequency components, the signal was rectified. Data were then band-pass filtered between 2 and 130 Hz and the power was calculated. Outliers larger than two times the standard deviation were removed. The EMG power was averaged between the two recorded channels and convolved with a hemodynamic response function. This regressor was standardized by dividing by the standard deviation and was used as a regressor for the GLM in the fMRI analysis. The GLM also contained a regressor for motor imagery blocks and a separate regressor for the instruction. Parameter estimates of movement (EMG) and imagery blocks were tested for significance with a *t*-test. Group analysis for significance of movement and imagery activity across subjects are reported at $p < 0.001$ uncorrected, cluster size larger than ten voxels.

2.4. EEG and ECoG measurement

EEG and ECoG data were acquired with a 128-channel recording system (Micromed, Treviso, Italy) with a 512 Hz sampling rate and 0.15–134.4 Hz band-pass filter. In the patient, arrays of ECoG electrodes were implanted subdurally for the localization of the epileptic seizure focus (for planning of surgical removal). These platinum electrodes had an inter electrode spacing of 0.5 or 1 cm and an exposed surface of 2.3 mm in diameter. Electrodes were localized from a CT scan and were projected to the cortical surface [18]. The EMG signal was measured from the right hand extensor digitorum communis and abductor pollicis brevis to control for EMG during motor imagery.

Signals were re-referenced to the common average of all EEG/ECoG electrodes and 2 s epochs were extracted from movement, imagery and rest blocks. Electrodes and epochs that showed eye blink, muscle (EEG) or epileptic (ECoG) artifacts were rejected. For each epoch, the power spectral density was calculated in steps of 1 Hz by Welch's method [19] with 1 s windows and a Hamming window to attenuate edge effects. Spectral power changes for movement and imagery compared to rest periods were then calculated. Power spectra of each epoch were normalized (by element-wise division) with respect to the mean power over all epochs at each frequency and were log-transformed. The log normalized power was then averaged for 8–24 Hz (EEG and ECoG) and for 65–95 Hz (ECoG). *T*-tests indicated whether differences between rest and (imagined) movement periods were significant, and results are reported at $p < 0.05$, Bonferroni corrected for the number of electrodes. For visualization purposes and to quantify the difference in power between movement and rest and motor imagery and rest, the r^2 was calculated [20]. The r^2 indicates the percentage of variance explained by different task conditions (movement versus rest and motor imagery versus rest).

2.5. BCI control

BCI2000 with the Sigfried module was used for the BCI task [21] in the patient. The ECoG activity from 65–95 Hz from the electrode closest to the area found in fMRI was used to control a cursor in a standard 2-target one-dimensional BCI task in which the cursor moves from left to right (in 2.3 s) to hit a target on the upper or lower right part of the screen [1]. The patient controlled the y-position of the cursor by imagining the same finger tapping as in the motor imagery task or relaxing during six sessions each of 4 min (174 trials).

3. Results

3.1. fMRI results

Healthy subjects group image analysis showed that during executed movement there was significant activity in the left M1, bilateral PMc, SMA, primary sensory areas, dorsal parietal cortex, cerebellum and basal ganglia, left thalamus and right inferior temporal cortex. A part of this network was also activated during imagined movement: during motor imagery there was significant activity in the left PMc, bilateral SMA, dorsal parietal cortex, basal ganglia and cerebellum. Surprisingly, no activity in M1 during motor imagery was found.

As individual subject analyses are more relevant for BCIs and group analyses could hide effects in individual subjects, we also calculated the significantly activated voxels ($t > 3.0$, $p < 0.001$ uncorrected) for each individual. We superimposed these individual maps, as shown in figure 1(A). The number of subjects in which a specific area was activated is shown in color. This figure shows a clear absence of activity during imagery in M1, an overlap for all 12 subjects in the PMc and for almost all subjects in the dorsal parietal area (max 10).

To more specifically test whether there was no significant activity in M1 during motor imagery, we defined M1 from the average anatomical scan by manual segmentation. Within the segmented M1, shown in figure 1(B), the number of significant voxels during imagery did not differ from zero (3 voxels on average, $t = 1.91$, $p = 0.08$). During movement there was significant activation in M1 across all subjects (49 voxels on average, $t = 29.11$, $p < 0.001$). Also, the fMRI signal change in M1 during imagery did not differ from zero ($t = -1.35$, $p = 0.20$), whereas during movement there was significant signal increase in M1 ($t = 11.47$, $p < 0.001$).

3.2. EEG results

Figure 1(C) shows that in EEG, there were significant decreases in power (8–24 Hz) during both movement and imagery compared to rest on contralateral electrodes. In 10 of 12 individual subjects, this decrease was significant ($p < 0.05$ Bonferroni corrected for multiple comparisons) in contralateral electrodes around sensorimotor cortex (C3, CP3, CCP3, CCP5). The other two subjects showed a power decrease during imagery in these electrodes, but this did not survive multiple comparison correction. These spectral power

decreases in contralateral sensorimotor rhythms are similar to those classically seen in other EEG-based BCI studies and this suggests that the motor imagery strategy used by the subjects could be used similarly to control an EEG-based BCI.

3.3. ECoG results and BCI performance

The ECoG data showed significant changes in power at low (8–24 Hz) and high frequencies (65–95 Hz) during motor execution and imagery. Figure 1(D) shows that during motor imagery high frequency power increases were localized specifically on the premotor area that showed significant fMRI activation. Electrical stimulation of these electrodes elicited no hand movement. Spectral power decreases in low frequencies were a bit more distributed around this area. Figure 1(D) shows that neither low nor high frequency changes were observed in M1.

The cursor in the BCI task was controlled by high frequency power changes from 65 to 95 Hz from the electrode on the premotor area that was found to be robustly activated by fMRI (indicated in figure 1(D)). On average, the patient performed the BCI task with 91% correctness (while 50% is chance level).

4. Discussion

This study investigated which brain areas were robustly activated during motor imagery and could be localized as a target for an invasive BCI. The fMRI results showed that during motor imagery there was robust activation of the dorsal premotor cortex (PMc) across individual subjects. This activity co-localized with a spectral power increase at high frequencies and a decrease at low frequency sensorimotor rhythms as measured with ECoG during the same task. The signal from this premotor area was then used to control a BCI and yielded very good performance (91%).

Previous BCI studies have generally focused on signals from M1 [22–24]. However, signals from other regions may be just as suitable to control a BCI [2]. While several fMRI studies have indicated that M1 may be activated during motor imagery, there is also a large amount of literature that suggests the opposite (for reviews see [9, 11]). In our study, we found no evidence for M1 activity during motor imagery. We did find activity in the PMc and previous studies have shown that the dorsal PMc is important for generating the motor plan, before the signal for movement execution is generated in M1 [25, 26]. The fMRI changes in the PMc co-localized well with the ECoG signal change in high frequencies, indicating that the signal we measure with fMRI is related to high frequency power change, as has also been shown in other studies [27–29]. Since the spectral power changes in high frequencies from this area yielded very good BCI performance, the results strongly suggest that fMRI localization of PMc for motor imagery is reliable enough for subsequent electrode positioning for a BCI implant.

In addition to the PMc, the dorsal parietal area was activated across almost all subjects during fMRI. Previous studies on motor imagery have suggested that this area

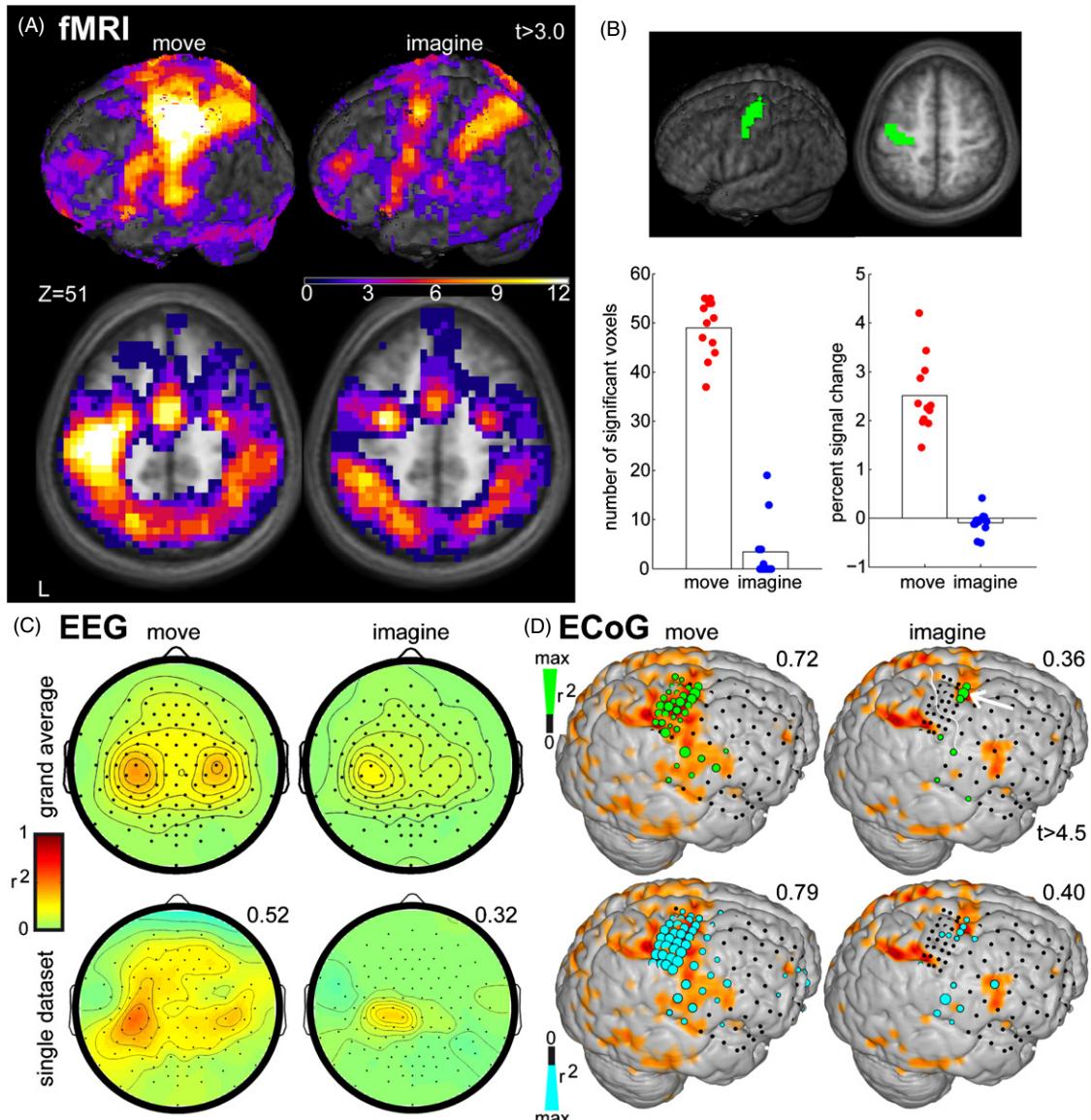


Figure 1. fMRI, EEG and ECoG results. (A) Significant fMRI activity ($t > 3.0$) was calculated for each individual during movement (left panel) and imagery (right panel) compared to rest. These maps are displayed superimposed, and the color scale indicates the number of subjects that showed significant activation in a region. Results are displayed on the average normalized anatomical scan of all 12 subjects. (B) The primary motor cortex was manually delineated on the average anatomical scan. Within this region, the number of significant voxels during movement (red) and imagery (blue) were calculated (left bar graph). We also calculated the percentage signal change during movement (red) and imagery (blue), displayed in the right bar graph. (C) The EEG data in the top panel show the grand average r^2 across all 12 subjects during movement (left panel) and imagery (right panel); the color scale ranges from 0 to 1. In the lower panel, a representative subject is shown; maximum r^2 values are denoted in the top right. (D) The ECoG data overlaid on the fMRI BOLD increases during movement (left panel) and imagery (right panel) compared to rest (orange, $t > 4.5$, $p_{\text{FWE corrected}} < 0.05$) on the surface rendering of the individual patient. ECoG spectral power increases during movement and imagery at high (65–95 Hz) frequencies are displayed in green in the top panel; decreases in low (8–24 Hz) frequencies are shown in cyan in the bottom panel. For significant electrodes, the size indicates the size of the r^2 , which is scaled to the maximum r^2 denoted at the top right. An arrow in the top-right panel indicates the electrode used for BCI control and a white line indicates the central sulcus.

is involved in sensorimotor mapping [26] or movement simulation [30], and patients with lesions in this area have impaired motor imagery capabilities [31]. Research in non-human primates has shown that signals from this area can be used to decode intended movement direction and are suitable to control a BCI [32], but since ECoG electrodes did not cover this area, we were unable to further explore the suitability of this area for ECoG motor imagery-based BCI control.

There are several possible explanations for the difference between this study and other BCI studies that do find M1 activation during motor imagery. For one, not many studies have corrected for (subtle) movements during imagery. In this study, movement was eliminated from imagery fMRI maps by including EMGs in the analysis directly. Secondly, M1 activity may be stronger when feedback is given as compared to activity during a localizer task [24]. Previous studies have indeed shown that attention can modulate the signal changes

during movement in M1 [33]. Lastly, motor imagery may differ from attempted movement: tetraplegic patients have successfully generated activity in M1 by *attempting* movement [34]. Whereas M1 may thus be suitable for BCI control, our fMRI results suggest that other areas, such as the dorsal premotor cortex, are more robust in their activation pattern and easy to localize in an individual subject. While ECoG results could only be collected in one patient, they confirmed that the fMRI results and signals from PMd resulted in successful BCI performance. Further ECoG studies are required to determine the generalizability of our findings across patients.

While fMRI indicated no activity in M1 during motor imagery, the EEG data showed spectral power decreases in sensorimotor rhythms that peaked around contralateral sensorimotor areas. Considering the ECoG data which showed low frequency spectral power change in PMc co-localized on the areas found by fMRI and also other studies that reported good co-localization between fMRI and low frequency power decrease [35, 36], it is unlikely that we measured signals from different areas with EEG and fMRI. The fact that parietal and premotor areas, specifically dorsal PMc, are adjacent to the central sulcus, and that the EEG signals exhibit an inherently lower spatial resolution than fMRI, may contribute to the apparent focus over primary sensorimotor areas that we saw on the scalp in this study. More complex EEG analysis methods or a different reference strategy such as a Laplacian, which is more sensitive to local changes [37], or an infinite reference [38] may be able to test this notion by teasing apart the signal from these different areas. We chose here for a simple analysis and common average reference, to show that our motor imagery task elicited EEG results that are comparable to those of other BCI studies.

In conclusion, this study suggests that for implanting an invasive BCI, the premotor cortex may be a more suitable target than the primary motor cortex. Furthermore, the match between the fMRI and ECoG data further confirms the reliability of PRESTO fMRI for preoperative localization of areas suitable for BCI implants [1].

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