Towards predicting ECoG-BCI performance: assessing the potential of scalp-EEG*

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Towards predicting ECoG-BCI performance: assessing the potential of scalp-EEG*

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Abstract

Objective. Implanted brain-computer interfaces (BCIs) employ neural signals to control a computer and may offer an alternative communication channel for people with locked-in syndrome (LIS). Promising results have been obtained using signals from the sensorimotor (SM) area. However, in earlier work on home-use of an electrocorticography (ECoG)-based BCI by people with LIS, we detected differences in ECoG-BCI performance, which were related to differences in the modulation of low frequency band (LFB) power in the SM area. For future clinical implementation of ECoG-BCIs, it will be crucial to determine whether reliable performance can be predicted before electrode implantation. To assess if non-invasive scalp-electroencephalography (EEG) could serve such prediction, we here investigated if EEG can detect the characteristics observed in the LFB modulation of ECoG signals. *Approach*. We included three participants with LIS of the earlier study, and a control group of 20 healthy participants. All participants performed a Rest task, and a Movement task involving actual (healthy) or attempted (LIS) hand movements, while their EEG signals were recorded. *Main results.* Data of the Rest task was used to determine signal-to-noise ratio, which showed a similar range for LIS and healthy participants. Using data of the Movement task, we selected seven EEG electrodes that showed a consistent movement-related decrease in beta power (13–30 Hz) across healthy participants. Within the EEG recordings of this subset of electrodes of two LIS participants, we recognized the phenomena reported earlier for the LFB in their ECoG recordings. Specifically, strong movement-related beta band suppression was observed in one, but not the other, LIS participant, and movement-related alpha band (8–12 Hz) suppression was practically absent in both. Results of the third LIS participant were inconclusive due to technical issues with the EEG recordings. *Significance*. Together, these findings support a potential role for scalp EEG in the presurgical assessment of ECoG-BCI candidates.

1. Introduction

Diseases such as amyotrophic lateral sclerosis (ALS), or events such as a brain-stem stroke, may cause severe paralysis and leave people effectively locked in their body: unable to move or speak, yet cognitively (relatively) unaffected (locked-in syndrome, LIS (Bauer *et al* 1979, Hayashi and Kato 1989)). For these people, brain-computer interfaces (BCIs) are being developed to restore communication abilities that were lost due to severe paralysis. By recording signals from the brain and by translating these into a control signal for a computer, BCIs can provide individuals with LIS a muscle-independent way of controlling communication software. A promising signal source for the control of such BCIs is the

sensorimotor (SM) cortex, where movement and attempted movement have been associated with a reproducible decrease in spectral power of the low frequencies (alpha [8–12 Hz] and beta [13–30 Hz] frequency bands; (Neuper and Pfurtscheller 2001a, Neuper *et al* 2006, Erbil and Ungan 2007) as well as with an increase in high frequency band power (Crone *et al* 1998, Ohara *et al* 2000, Miller *et al* 2007, Ball *et al* 2008, van den Boom *et al* 2021).

In the framework of the Utrecht Neural Prosthesis (UNP) study, people with LIS have been surgically implanted with a BCI, aiming to provide participants with a new and brain-based method of communication for home use (Vansteensel *et al* 2016, Pels *et al* 2019). The implantable BCI consists of subdural electrocorticography (ECoG) electrodes placed on the surface of the SM area of the brain and an amplifier/transmitter device that is placed subcutaneously in the chest. Using attempted movements of the hand, participants generate changes in low frequency band (LFB) and high-frequency band (HFB) power in the SM area, which are converted into a brain-click for control of communication software. In an earlier study, we investigated LFB and HFB features of two UNP-study participants (i.e. UNP1 and UNP4) with LIS (Freudenburg *et al* 2019) and compared these features to those of a group of able-bodied people with epilepsy who received a subchronic implant with ECoG electrodes for diagnostic purposes. Both participants with LIS showed clear changes in HFB power in the SM areas upon attempted hand movement, similar to that observed during hand movement in the able-bodied group. However, in only one LIS participant (UNP1) the high-frequency change was accompanied by clear changes in LFB power (as also observed in the able-bodied group), which resulted in successful BCI performance and home use that has lasted for several years already (Vansteensel *et al* 2016, Pels *et al* 2019). The other participant with LIS (UNP4), however, did not exhibit a reliable decrease in LFB power, and the BCI did not work as efficiently.

For future clinical application of BCIs based on implanted ECoG electrodes, it will be important to predict whether or not a certain individual has a high chance of achieving accurate control over the BCI before deciding to perform surgery. This pre-implantation assessment is ideally accomplished using non-invasive neural signal recording modalities. Measurements from the scalp (electroencephalography, EEG) could provide a rapid and easy approach to determine the quality of the neural signal changes prior to BCI implantation. However, whether EEG could be used as a predictive tool for this purpose remains to be assessed.

In this study, we aimed to determine whether the interindividual differences we observed earlier in the LFBs of the ECoG signal of the UNP-participants (Freudenburg *et al* 2019) can be detected using non-invasive EEG measurements. In other words, we assessed if scalp EEG recordings can detect similar anomalies in the neural activity of individuals with severe motor-impairment as observed with ECoG. To this purpose, we compared EEG LFB power modulation associated with attempted hand movement of the UNP participants with LIS with that of a cohort of healthy participants who performed an executed hand movement task. The UNP participants with LIS of the current study included the two individuals described above (UNP1 and UNP4) and a third individual with LIS due to ALS (UNP5), all of whom had an implanted ECoG-BCI system and used a combination of LFB and HFB features for ECoG-based BCI control. We primarily focused on the alpha and beta bands of the EEG, as these frequencies showed differential activity in the participants with LIS, and since recordings of HFB power with EEG may be unreliable (Darvas *et al* 2010, Nottage and Horder 2015). The results of this study may be relevant for future research on and clinical implementation of implanted BCIs.

2. Experimental procedures

2.1. Subjects

2.1.1. Healthy participants

Twenty healthy, right-handed volunteers participated in the study (handedness as measured by Edinburgh Handedness Inventory, M = 0.89, SD = 0.13, age ranged from 19 to 65 with M = 41.3 yr, SD = 16.1 yr, nine female). The study was assessed by the Medical Research Ethics Committee (MREC) Utrecht, who confirmed that the Medical Research Involving Human Subjects Act (WMO) did not apply and MREC approval was therefore not required. Yet, all volunteers gave their written consent after a detailed written and oral explanation of the procedure. No participant reported any relevant neurological or psychiatric disorders. All participants had normal or corrected to normal vision.

2.1.2. Participants with LIS

EEG recordings from three participants with LIS were acquired as part of their participation in the UNP study. The UNP study (Clinicaltrials.gov NCT02224469) was approved by the MREC Utrecht (NL40539.041.12) and was conducted according to the Declaration of Helsinki (2013). Informed consent was obtained using a dedicated procedure, as defined earlier (Vansteensel *et al* 2016). Two participants with LIS, UNP1 and UNP4, have been described in previous studies (Vansteensel *et al* 2016, Freudenburg *et al* 2019, Pels *et al* 2019, Leinders *et al* 2020).

Briefly, UNP1 is a woman, aged 63 years at the time of the EEG data acquisition in 2020, who was diagnosed with ALS in 2008. She is quadriplegic and anarthric, and receives tracheostomy invasive ventilation. She was implanted with the UNP-BCI (i.e. Resume II, Activa PC + S, Medtronic, both

off-label use) in 2015. At the time of the EEG recording, she only had functional residual movement in the corner of her mouth, which she could use to answer closed questions. In addition, she used the UNP-BCI for caregiver calling and communication.

UNP4, also a woman, has been severely paralyzed and anarthric as a result of a brainstem stroke in 2004. She was implanted with the UNP-BCI in 2017. She was 42 years old at the time of EEG acquisition. For communication, she used a head switch to control communication software, as well as eye and head movements to answer closed questions.

UNP5 is a man who was diagnosed with ALS in 2011. He is quadriplegic and anarthric, receives tracheostomy invasive ventilation, and uses an eye gaze device for communication with his family and caregivers, as well as small movements of the jaw to answer closed questions. He was implanted with the UNP-BCI in the beginning of 2020. He was 65 years old at the time of the EEG recordings.

2.2. Experimental paradigm

2.2.1. Movement task

All participants performed a task consisting of alternating 30 s blocks of finger tapping with the right hand (attempted finger tapping in the case of LIS participants) and rest. Instructions were visually presented on a computer screen. During the finger tapping blocks, participants were asked to (attempt to) touch their thumb with their other fingers, in random order, at a comfortable pace. During the rest blocks, participants were instructed to quietly watch the screen and think of nothing in particular. Each participant performed three runs of the Movement task within the same recording session. Each run had a duration of 5.5 min, starting with a 30 s block of rest. Data for one run in one participant had a shorter duration of 4 min.

2.2.2. Rest task

All participants also performed a resting-state task in which they quietly gazed at an image of a blue, open circle on a computer screen and were instructed to think of nothing in particular. Per participant, three 5 min runs were recorded within the same session.

2.3. EEG recording and pre-processing

The EEG data was recorded using an Easy-Cap^{TM} (Easycap, Germany), with 84 electrodes arranged according to the international 10-10 system. Additionally, two electrodes were placed close to the eyes to record eye movements. The linked mastoids were used as references. The EEG signal was recorded at a 512 Hz sampling rate, and with a high-pass filter of 0.15 Hz and a low-pass filter of 134.4 Hz (LTM 64, Micromed, Treviso, Italy). Conductive gel was applied in each of the electrode holes to ensure contact with the scalp and high-quality recordings, by an experienced clinician of the clinical neurophysiology department. Note that we did not acquire ECoG recordings simultaneously with EEG.

The EEG recordings were filtered using a 4th order Butterworth filter in the range of 0.5–120 Hz to remove high-frequency artefacts and signal drift. Powerline frequency was removed with a notch filter between 48 and 52 Hz. To eliminate eye and muscle artefacts, we manually identified and removed noisy components using the ICA procedure available in the Fieldtrip toolbox (Oostenveld *et al* 2011). Bad channels were manually selected using the *ft_rejectvisual* function and their recordings interpolated using the distance method based on a template available in Fieldtrip. Common average re-referencing of all channels was done after removal of bad channels. For the Movement task, data was cut into trials of 30 s of movement and rest. For the Rest task, data was cut into overlapping trials of 2 s (75% overlap) after which bad trials were removed using the *ft_rejectvisual* function. For the sake of reproducibility, the processing pipeline was documented using the *ft_reproducescript* function.

2.4. Signal analysis

2.4.1. Signal quality

As an initial signal assessment of signal quality, we computed the signal-to-noise ratio (SNR) of the Rest task data as follows:

$$SNR = 10\log\left(\frac{P_{13-30\,\mathrm{Hz}}}{P_{52-100\,\mathrm{Hz}}}\right). \quad (1)$$

2.4.2. (Attempted) movement-related changes in power

To investigate the (attempted) movement-induced modulation of neural activity of all participants and all electrodes, we computed the coefficient of determination (signed R squared or R2) of the Movement task, in two frequency bands of interest, the beta band (13–30 Hz) and the alpha band (8–12 Hz), as follows. For every block, spectral power (1 Hz bins, only the first 29 s of each block were used to avoid possible artefacts related to the transition between conditions) was computed using the multitaper method (Mitra and Pesaran 1999). A frequency resolution of five cycles per time window was used, with the time-interval of interest set at 100 ms. Responses in the alpha and beta bands over time were computed as the sum over the log of the time varying power for the two frequency bands. We cut the 29 s blocks further into overlapping trials of 5 s (50% overlap) and defined three movement related features: (a) a decrease in beta band power during movement trials versus rest, (b) a decrease in alpha band power during movement trials versus rest and (c) an increase in beta band power during the first 5 s after a movement trial ended (i.e. the rebound period) versus rest. In all cases, rest was taken as the period after the rebound time (i.e. from 5 s after the onset until the end of a 29 s rest block). For each of these features, we computed

the coefficient of determination (signed R2 value) per electrode per subject.

Based on the Movement task R2 values of all electrodes of the healthy participants, we selected a subset of electrodes that best represented motor-related signal changes. Because the earlier findings in the ECoG data of the LIS participants were based on left-hemisphere electrodes (Freudenburg *et al* 2019), we here only considered electrodes over the contralateral (i.e. left) hemisphere, and selected those electrodes that showed a significant (p value < 0.05 uncorrected, as this step was only used for electrode selection) movement-related decrease in beta power in most healthy participants. This subset of electrodes was used to compare alpha and beta band R2 values between healthy participants and participants with LIS.

We assessed if the participants with LIS showed any significant changes in the R2 values for alpha and beta band power. For that purpose, we corrected for multiple comparisons using a Bonferroni correction over the number of channels in the selected electrode set.

We also computed the variability of the R2 values for the participants with LIS, using a bootstrap analysis with 100 repetitions, where each time R2 was computed from ten random 5 sec samples of rest (without the 5 s rebound period) and movement trials.

2.4.3. Power spectral density

For a closer evaluation of the spectral features, we computed the Power Spectral Density (PSD) over the entire Rest task and over the move and rest blocks of the Movement task, for all participants. As channel C3 is typically considered to be the best position for recording activity of the left primary motor cortex (Stancák and Pfurtscheller 1996, Wang *et al* 2006, Daskalakis *et al* 2008, Rogasch *et al* 2013, Ives-Deliperi and Butler 2018, Ogata *et al* 2019), we selected this channel for the PSD computation, which was accomplished using Welch method with a window length of 1 s and window overlap ratio of 50%.

2.4.4. Beta rebound

We investigated the presence of any post-movement rebound effects in the beta and alpha band. Time frequency traces of beta band power of the Movement task were smoothed with a smoothing factor of 10 (corresponding to 1 s). Grand-average beta power time courses (mean over participants for the healthy participants) were obtained. The power of the rebound period relative to the remainder of the rest trials (referred to as the baseline period from now on) was defined as the percentage deviation of the power A_i at time point i from baseline average power B, according to the following equation:

$$RA = \frac{(A_i - B)}{B * 100}. \quad (2)$$

For this computation, the baseline period was defined as the part of the rest blocks after the rebound period (from 5 s to the end of the 29 s rest blocks in the Movement task). To determine statistical significance of any changes in the grand average beta power during the rebound period, 95% confidence intervals around the average relative power values were calculated by applying a t-percentile bootstrap statistic to the power values (Graimann *et al* 2002).

3. Results

3.1. Signal quality

Assessment of the signal quality of each participant, using the SNR of the Rest task, showed that there was quite some variability across electrodes and across participants (figure 1). Although several healthy participants, as well as UNP5, showed, on average, relatively low SNR values, none of the participants were excluded based on this evaluation.

3.2. (Attempted) movement-related changes in power

Overall, clear movement-related beta band responses occurred in central areas over the ipsilateral and contralateral hemisphere (figure 2(a)). We selected the most relevant electrodes for further analysis based on the movement-related decrease in beta band power. There were seven channels over the contralateral, left, hemisphere (C3, C1, CP3, CP1, P3, P1 and FC1) where beta band suppression during movement compared to rest showed a significant ($p < 0.05$, uncorrected) effect in at least 85% (17 out of 20) healthy participants (figure 2(a)). Specifically, beta band responses of these electrodes were found to be significant in 90% (C3), 90% (C1), 100% (CP3), 90% (CP1), 90% (P3), 85% (P1) and 95% (FC1) of the healthy participants, respectively. The mean R2 values over all healthy participants for these electrodes were also among the most negative values (figure 2(b)). In sum, a total of 12 channels did not show any significant beta suppression, distributed across four participants.

For the alpha band, the R2 values of these electrodes were found to be significant in at least 60% of the healthy participants. Specifically, electrodes C3, C1, CP3, CP1, P3, P1, and FC1 were found to be significant ($p < 0.05$, uncorrected) in 75%, 80%, 80%, 60%, 65%, 60% and 80% of the healthy participants respectively (supplementary figure 1). A total of 34 channels did not show significant alpha suppression, distributed across 12 participants. Out of these 12, 2 participants were consistently non-significant for all channels.

For the seven selected SM electrodes, we subsequently compared the movement-related changes in alpha and beta band power (R2 values) of the participants with LIS to those of the healthy participants (figure 3(a)). For the beta band, the R2 values of all selected electrodes of UNP1 were in the same range

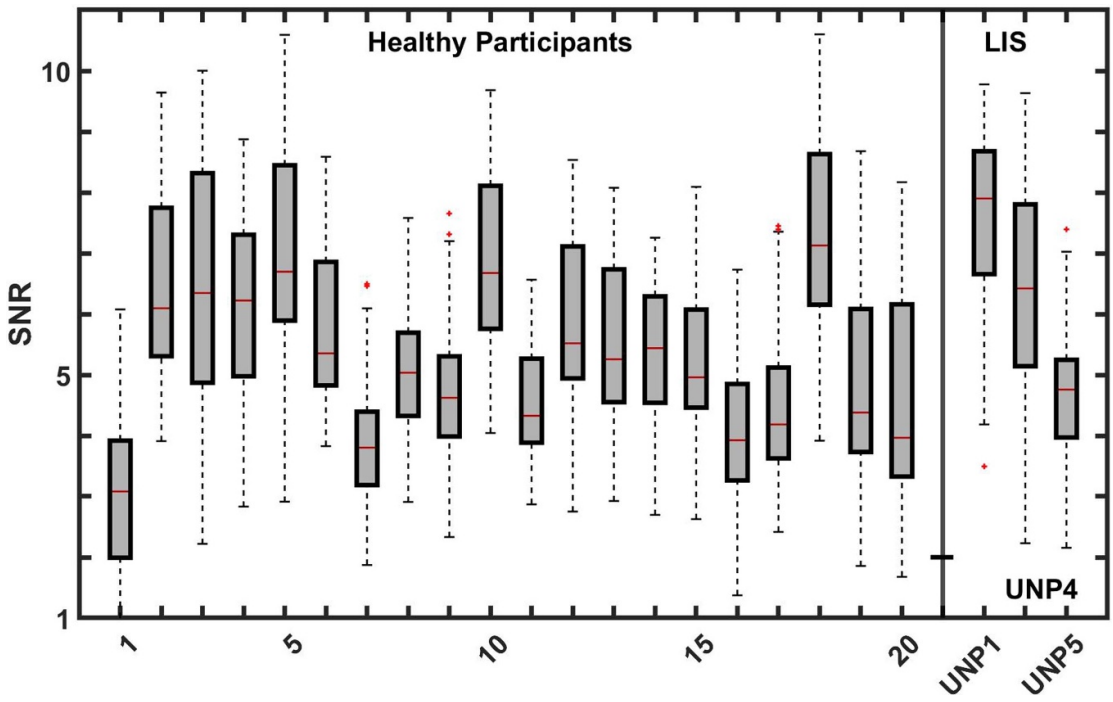

Figure 1. Signal to noise ratio. Boxplot of the signal to noise ratio (mean over all included EEG channels) of the Rest task, for each of the 20 healthy participants and 3 participants with LIS. For each participant, the median is given (red horizontal line), as well as the interquartile range (box), minimum and maximum values (dashed whiskers), and outliers (red crosses).

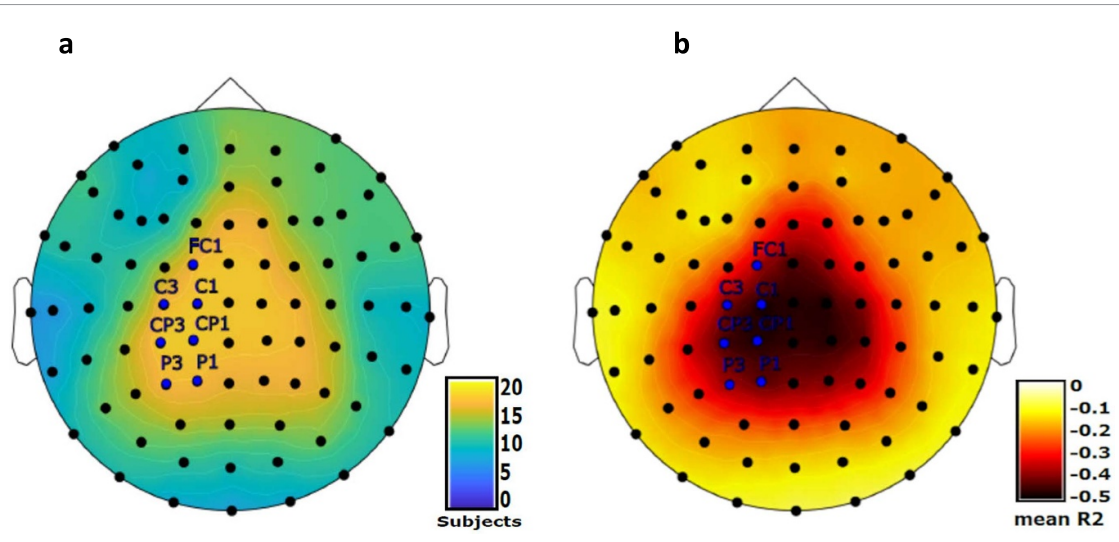

Figure 2. Electrode selection. (a) The seven electrodes over the left hemisphere marked with their electrode name were selected for the regression analysis as they showed a significant movement-related change in beta band power in most healthy participants, and are therefore considered to be the most representative of motor-related signal changes. The color scale indicates the number of participants with a significant beta power R2 value (uncorrected). (b) Mean beta power R2 values over healthy participants.

as those obtained for the healthy participants, ranging between −0.05 and −0.69 (M = −0.35; SD = 0.23, all selected electrodes significant at $p < 0.001$ (corrected), except CP1). Two electrodes of UNP1 showed especially large responses (C3: mean R2 value −0.69; CP3: mean R2 value −0.64; figure 3(a)). For UNP4, however, all selected electrodes showed a relatively small R2 value, mostly within the 25% least negative values obtained for healthy individuals, ranging between −0.12 and −0.28 (M = −0.22; SD = 0.05; all significant at $p < 0.01$ (corrected)) over the subset of selected electrodes. For UNP5, the beta response was only significant in CP3 ($p < 0.001$, corrected) out of the selected electrodes, but showed an opposite effect. Most R2 values of UNP5 were outside of the range obtained for healthy controls.

For the alpha band, only P1 of UNP1 showed a significant R2 value, but the effect was opposite to that typically observed for healthy participants. None of the other selected electrodes of the participants with

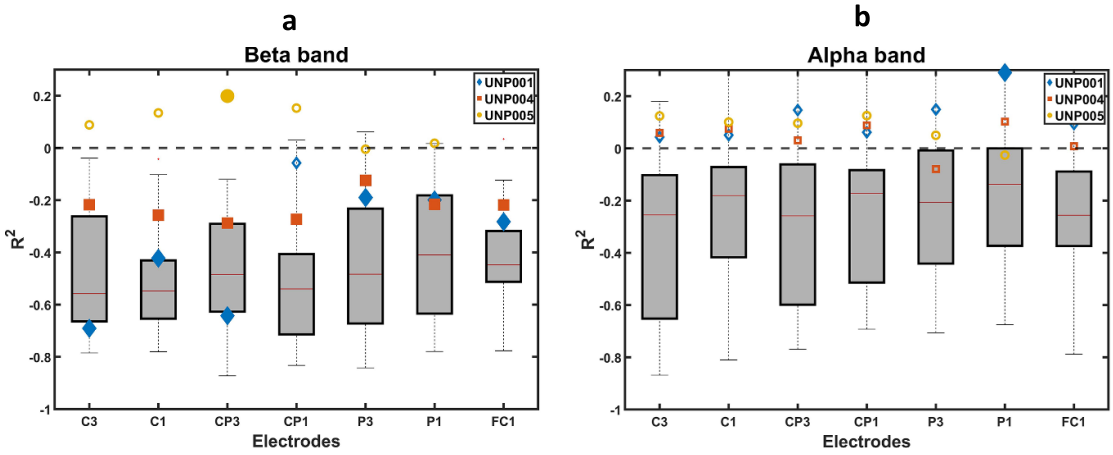

Figure 3. Task-related modulation of power in the low frequency bands. Grey boxplots represent the range of signed R2 values of beta (a) and alpha (b) band power responses in healthy participants, for each of the seven selected electrodes over the left hemisphere. For each of the electrodes, the respective R2 values of the participants with LIS are indicated with a blue diamond (UNP1), orange square (UNP4) or yellow circle (UNP5). Values that were significant for the participants with LIS (after correcting for multiple comparisons over the selected channels using Bonferroni correction) are indicated with a filled, larger symbol.

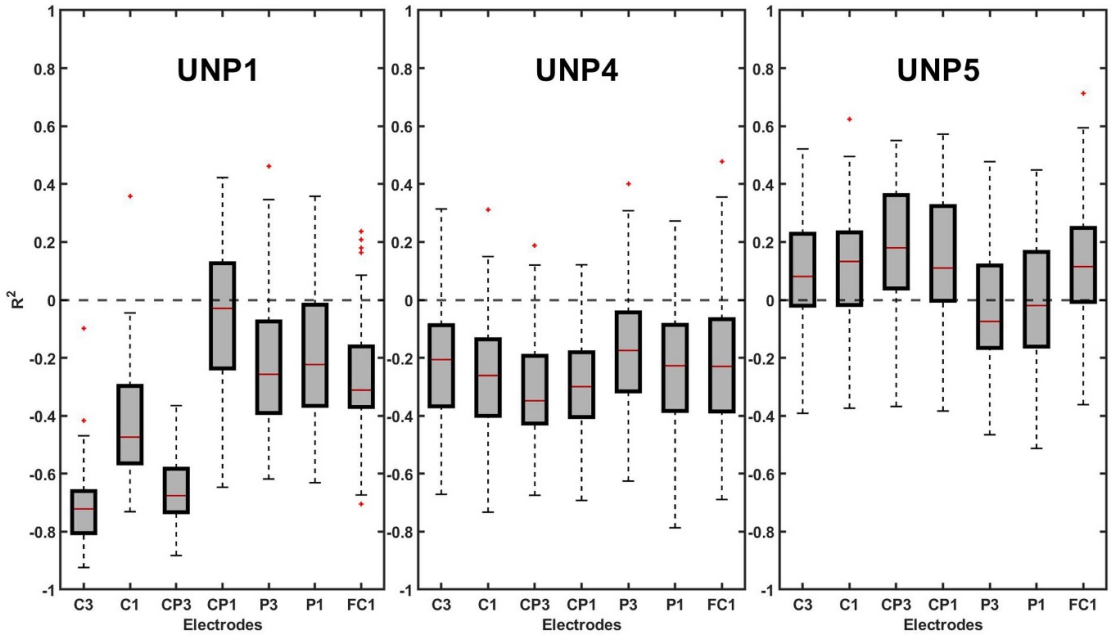

Figure 4. Variance boxplots of the R2 values in beta band power over different runs for each LIS participant, for the selected subset of electrodes.

LIS were found to show a significant R2 value for the alpha band (figure 3(b)). All R2 values of the LIS participants fell within the range found for healthy participants, albeit mostly among the 25% least negative values of this group.

For the subset of seven electrodes of the LIS participants, we estimated the variability across runs of the R2 values of beta power decrease (figure 4). The two channels with the most negative mean beta R2 values of UNP1 were also the ones with the lowest variability (i.e. channel C3 (SD 0.1) and CP3 (SD 0.13) in figure 4, top panel). For all other electrodes of the three participants with LIS the variability was higher, with SDs in the range of 0.15–0.25. The same assessment was done for the alpha band (supplementary figure 2).

3.3. Power spectral density

Investigation of the mean power spectrum of C3, the electrode with the most negative median signed R2 value in the beta band across healthy participants, showed a clear modulation in beta band activity during the Movement task of the healthy participants (figure 5). This modulation was also observed in the power spectrum of UNP1, but seemed very weak or absent in UNP4 and UNP5. In addition, while a modulation in the alpha band was clearly present in the mean power spectrum of the healthy participants,

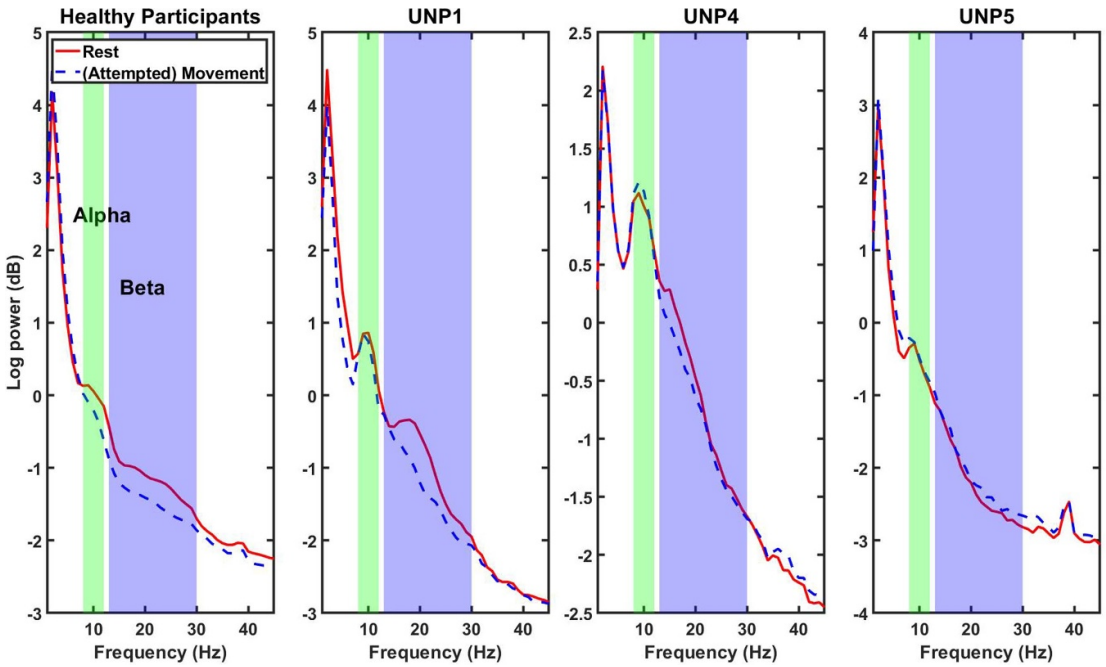

Figure 5. Power spectral density plots for channel C3, for healthy participants (mean over 20 healthy participants) and the three participants with LIS. Power Spectral Densities are shown for both rest and movement trials of the Movement task, for a range of 1–45 Hz. The alpha frequency band is indicated by green shading, the beta frequency range by blue shading. The peak in the delta (0–4 Hz) frequency range is most likely an effect of the 0.5 Hz high pass filter that was applied during the analysis.

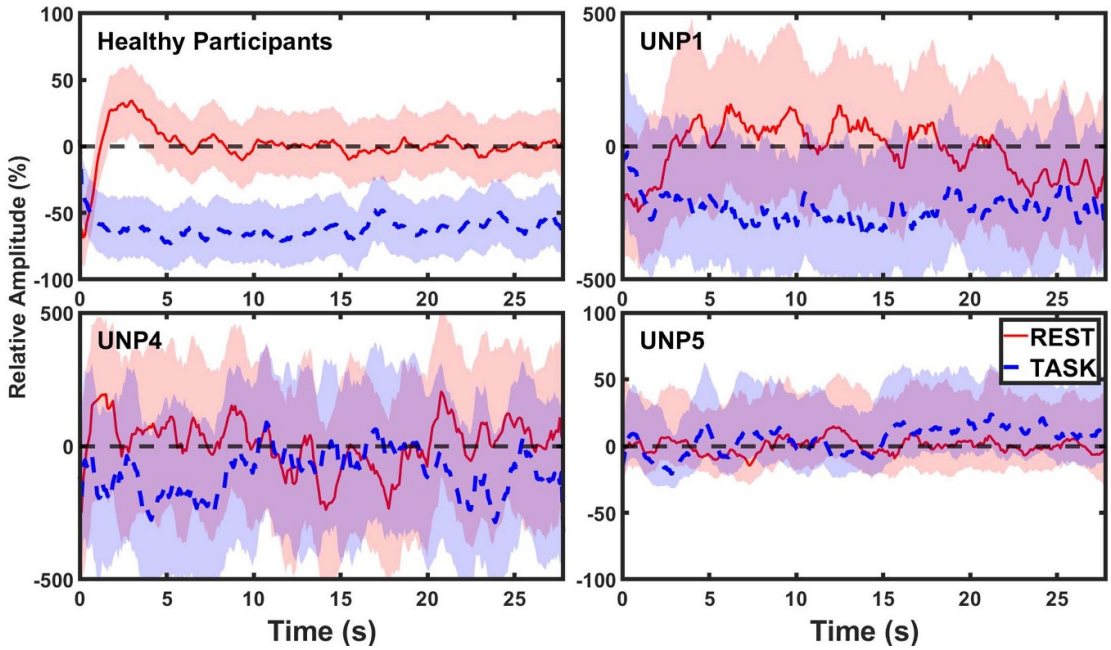

Figure 6. Power traces over time (solid red: rest, dashed blue: attempted movement) of the beta band recorded from channel C3, for all healthy participants (grand-average over participants, n = 20) and each of the participants with LIS. Time = 0 represents the cue to start or stop moving. Note the different scales of the *y* axis for different panels, which represent relative amplitude defined as percentage deviation from the power of the baseline period.

none of the participants with LIS exhibited this effect.

3.4. Beta rebound

In the beta power traces over time (mean over trials and healthy participants) of the movement and rest trials of the Movement task, a rebound response could be observed during approximately the first 5 s of the rest trials, in several of the selected electrodes (figure 6, showing traces for C3). Within the subset of selected electrodes, the mean rebound response for the healthy participants showed a significant increase compared to baseline during the 5 s rebound period (95% confidence interval) for channels C3, CP3 and

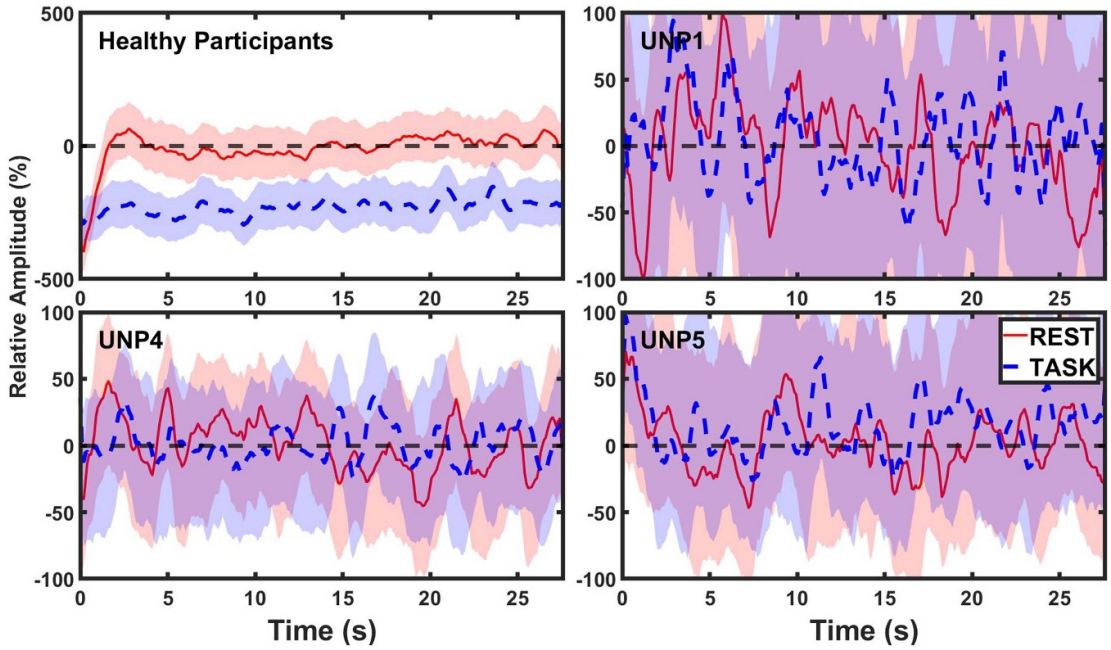

Figure 7. Power traces over time (solid red: rest, dashed blue: attempted movement) of the alpha band recorded from channel C3, for all healthy participants (grand-average over participants, n = 20) and each of the UNP participants. Time = 0 represents the cue to start or stop moving. Note the different scales of the *y* axis for different panels, which represent relative amplitude defined as percentage deviation from the power of the baseline period.

FC1. Notably, although a stable difference between movement and rest trials was observed for (almost) the entire duration of the trial in UNP1, a rebound response could not be clearly observed. Also UNP4 and UNP5 did not show a beta rebound effect in any of the electrodes. Note that for UNP4, visual inspection of the beta trace suggests a beta power difference between attempted hand movement and rest in the first 10 s (figure 6, panel UNP4), which may indicate that there is a short-lasting effect. However, the R2 values for only the first 10 s were comparable for those of the entire time window of the trial, for both participants (results not shown).

Alpha power traces (mean over trials for participants with LIS and over healthy participants) over time showed no significant rebound response in either healthy participants or participants with LIS (figure 7, showing traces for C3). Additionally, while a stable and significant decrease in alpha trace during movement could be observed for the healthy participants, none of the participants with LIS showed an alpha decrease during movement compared to rest.

4. Discussion

In the current study, EEG signals from three individuals with LIS were compared to those of 20 healthy participants, to investigate to what extent previously observed interindividual differences in ECoG LFB characteristics of neural signals from the SM cortex of the LIS participants (Freudenburg *et al* 2019) can be identified using scalp EEG. Our data revealed that most of the earlier-reported features observed in the ECoG signal of the LIS participants could also be observed with EEG, despite the smaller signal-to-noise-ratio of EEG compared to that of ECoG (Ball *et al* 2009), and despite the presence of implanted ECoG electrodes that potentially affected the EEG scalp recordings (Lanfer *et al* 2013, von Ellenrieder *et al* 2014).

In the EEG of healthy volunteers, we observed a clear movement-associated suppression of power in a subset of electrodes around the SM cortex in the alpha and beta frequency bands, as well as a clear rebound response in the beta band during the first 5 s after a movement trial. Suppression in both frequency bands was observed in both the contralateral and the ipsilateral hemisphere, and was sustained over the duration of the movement trial. These results were well in line with those reported in previous studies (Pfurtscheller and Lopes da Silva 1999, McFarland *et al* 2000, Neuper and Pfurtscheller 2001b, Erbil and Ungan 2007).

Earlier, we reported that the ECoG signal of UNP1 showed a clear and strong attempted-movement-related decrease in power in the LFB (6–30 Hz). Importantly, this modulation was limited to beta frequencies (19–30 Hz; Freudenburg *et al* 2019). In the current study, the EEG data of UNP1 revealed that two of the seven selected electrodes (i.e. C3 and CP3) in the contralateral (left) hemisphere showed a strong decrease in beta band power during attempted hand movement, with R2 values among the most negative ranges observed for healthy participants. Of these electrodes, C3 is the site classically associated with hand movement

responses in EEG (Stancák and Pfurtscheller 1996, Wang *et al* 2006, Daskalakis *et al* 2008, Rogasch *et al* 2013, Ives-Deliperi and Butler 2018, Ogata *et al* 2019) and signals from this electrode likely correspond most closely to the ECoG electrode pair over the hand-knob area used for BCI control by UNP1. In correspondence with the ECoG findings, responses in C3 and CP3 for UNP1 also showed relatively little variance across different runs of the Movement task. The R2 values of the other five SM electrodes of UNP1 were closer to zero, but still mostly within the range of values observed in healthy participants. Also, for UNP4, EEG results were in line with the ECoG findings in that all seven selected SM electrodes showed only small decreases in beta band power. However, and in contrast to the ECoG findings of our earlier study (Freudenburg *et al* 2019), the R2 values of UNP4 did fall within the range of values obtained for the healthy participants (albeit among the smallest values obtained (i.e. closer to zero)).

Interestingly, the ECoG study of (Freudenburg *et al* 2019) reported that for UNP1, alpha band power showed a much weaker and less consistent modulation than that of the beta band (figure 2 of that paper), and, when looking only at the oscillatory components, alpha band modulation in UNP1 seemed absent (figure 6 of that paper). For UNP4, ECoG-alpha power modulation was weak. Similar to these findings, neither UNP1 nor UNP4 showed a significant movement-related suppression in alpha band power of the EEG, whereas this effect was observed in many healthy participants, albeit less consistently than that of the beta band. Note that both UNP1 and UNP4 did show a clear peak in the alpha frequency band, but that attempted-movement-induced alpha power suppression was absent or weak. In (Freudenburg *et al* 2019), the authors argued that the absence of movement-related modulation in the power of this frequency band could be explained by the fact that the specific area of the SM cortex covered by the electrode strip may not show this modulation. In the current study, however, the subset of seven selected electrodes covered a large area of the SM cortex and is therefore more likely to capture any movement-related modulation in alpha band power. These findings therefore suggest that the lack, or weakness, of alpha power modulation is not limited specifically to a subsection of the SM cortex but may be a more general feature of the SM cortex of the respective participants with LIS. Interestingly, also an earlier study reported that severely motor-impaired people failed to exhibit a consistent suppression in the alpha band (Höhne *et al* 2014). Notably, alterations in (global) resting state alpha power have been associated with cognitive impairment (see for a meta-analysis (Lejko *et al* 2020)). Specifically, the magnitude of resting state alpha activity is lower in people with cognitive impairment than in healthy individuals, and during the execution of for example working memory or attention tasks, modulation of alpha power is smaller. This raises the question if the lack of *attempted-movement* related changes in alpha power in the SM areas of UNP1 and UNP4 is associated with impaired cognition. We consider this unlikely, as both participants showed a very clear alpha peak in their power spectrum. In addition, all participants were evaluated by a neuropsychologist before the implantation of the UNP-BCI (see Vansteensel *et al* (2016) for details; for UNP1, this evaluation was repeated in 2020 [several weeks before the EEG measurements] because of the replacement of the amplifier/transmitter device). In these evaluations, no signs of cognitive impairment were found. Clearly, more research is needed to investigate the generalizability and the neurophysiological basis of the lack of alpha modulation in the SM areas we observed in two individuals with LIS, and to characterize any effects of ALS or brainstem stroke on this feature.

The results obtained with UNP5 were inconclusive. Importantly, this participant has shown clear motor-related changes in the ECoG signal, in both the low (supplementary figure 3) and high frequency bands. In the current study, however, none of the seven selected electrodes showed a significant decrease in alpha or beta band power and the power spectrum of C3 did not show a clear alpha or beta peak. The absence of these well-known baseline and motor-related features in the EEG of UNP5, and the apparent lack of consistency between EEG and ECoG signals of this participant is most likely caused by the important difficulties with acquiring high quality EEG data with this participant. First, there were difficulties fitting the EEG cap, and due to specific characteristics of the skin (thick and oily), noise levels may have increased, resulting in a relatively low SNR (Kappenman and Luck 2010), although the size of the EEG signal was not markedly reduced. Second, on the day before the EEG measurement, UNP5 received medical treatment unrelated to his research participation, which included midazolam sedation. Although UNP5 seemed attentive during the EEG session, it cannot be excluded that his level of functioning was suboptimal due to the medical procedures of the previous day. In addition, midazolam is known to affect EEG signals for hours after administration in healthy people (Milligan *et al* 1989, Veselis *et al* 1991, Hotz *et al* 2000) and there may have been some remaining effect on the EEG signals of UNP5 on the day of the EEG measurement.

Taken together, the results of this study suggest that LFB SM signal characteristics can be observed in both the EEG and the ECoG signals of people with LIS. Indeed, we observed high R2 values in the beta band for the UNP participant who also had strong LFB modulation in the ECoG signal, and the most reliable ECoG-BCI performance. In addition, the weak beta modulation of UNP4, and the weak

alpha modulation of UNP1 and UNP4 were observed in both EEG and ECoG. Although these findings are in line with the notion that the strength of LFB EEG modulation may reflect the strength of ECoG LFB modulation, they clearly need to be validated with more cases. This is especially relevant for situations in which EEG LFB R2 values are closer to zero. In these cases, several causes should be considered, including neurophysiological pathology (as proposed for UNP4; Freudenburg *et al* 2019), suboptimal data quality (as for UNP5), and interindividual variability. Indeed, based on EEG work, it has been suggested that a non-negligible part of the population is BCI-inefficient (Sannelli *et al* 2019, Zhang *et al* 2020) and that an estimated 25% does not reliably show a significant movement-related beta suppression in their EEG. More data will be needed to draw definitive conclusions on the predictive value of scalp EEG recordings for ECoG BCI performance.

The present work has several limitations. First, we studied only a very limited number of participants with LIS, who also had heterogeneous etiologies. Although this low number of participants is a logical consequence of the limited number of people implanted with ECoG electrodes worldwide, it will be important to eventually confirm our findings with a larger sample. Second, we acquired limited data per participant. For an optimal comparison between ECoG and EEG data, we chose to use the same Movement task design as used earlier in the ECoG study (Freudenburg *et al* 2019). Although the number of trials was lower than typically used for EEG studies, we observed a clear correspondence between EEG and ECoG data for two of the participants with LIS, whereas this correspondence was likely negatively affected by technical difficulties for a third participant. It will be interesting to perform a more in-depth investigation of the characteristics of the SM neural signals with a larger number of trials. Third, we used the same frequency bands for the analysis of all participants. This approach may have induced some variance, since several studies have indicated that the center frequency of the alpha and beta peaks in the power spectrum may differ between individuals (van Albada and Robinson 2013, Haegens *et al* 2014). Future investigations may benefit from more subject-specific approach, such as recent attempts to characterize power spectra by their putative oscillatory peaks (Donoghue *et al* 2020). Finally, in this study, we only looked at the modulation of neural activity in two frequency bands (beta and alpha). The ECoG study of (Freudenburg *et al* 2019) also investigated high frequency band power (31–100 Hz). Importantly, one of the acknowledged issues with EEG is its high noise due to artefact sources, such as muscle activity in the scalp, face and neck, which are especially of concern in the higher frequency ranges. Therefore, recording of the HFB power with EEG cannot be considered reliable (Darvas *et al* 2010, Nottage and Horder 2015) and this frequency band is typically studied using implanted electrodes. Although earlier reports do suggest that HFB power changes can also be observed using EEG (Ball *et al* 2008, Darvas *et al* 2010), the experimental design for these respective studies allowed for collection of a larger number of trials to optimize the SNR (between 100 and 600 trials per subject). In our case, the study was designed to resemble the design of (Freudenburg *et al* 2019) and 15 movement trials were collected per subject. Therefore, we did not include the analysis of the high frequency band in our study. Importantly, due to the focus on alpha and beta band power in the current EEG study, our conclusions about the predictive potential of EEG for ECoG-based BCI performance are therefore limited to BCI control that (partially) relies on these LFB features.

5. Conclusion

The findings of this study suggest that scalp EEG recordings of people with LIS may reflect LFB features that correspond to those obtained with implanted ECoG electrodes. These findings call for more research on the correspondence between EEG and ECoG features within the same individual and on the predictive value of a presurgical EEG for implanted ECoG BCI performance.

Data availability statement

The data generated and/or analysed during the current study are not publicly available for legal/ethical reasons but are available from the corresponding author on reasonable request.

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Conflict of interest

The authors report no conflicts of interest.

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References

Ball T, Demandt E, Mutschler I, Neitzel E, Mehring C, Vogt K, Aertsen A and Schulze-Bonhage A 2008 Movement related activity in the high gamma range of the human EEG *NeuroImage* **41** 302–10

Ball T, Kern M, Mutschler I, Aertsen A and Schulze-Bonhage A 2009 Signal quality of simultaneously recorded invasive and non-invasive EEG *NeuroImage* **46** 708–16

Bauer G, Gerstenbrand F and Rumpl E 1979 Varieties of the locked-in syndrome *J. Neurol.* **221** 77–91

Crone N E, Miglioretti D L, Gordon B and Lesser R P 1998 Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis. II. Event-related synchronization in the gamma band *Brain* **121** 2301–15

Darvas F, Scherer R, Ojemann J G, Rao R P, Miller K J and Sorensen L B 2010 High gamma mapping using EEG *NeuroImage* **49** 930–8

Daskalakis Z J, Farzan F, Barr M S, Maller J J, Chen R and Fitzgerald P B 2008 Long-interval cortical inhibition from the dorsolateral prefrontal cortex: a TMS-EEG study *Neuropsychopharmacology* **33** 2860–9

Declaration of Helsinki 2013 *WMA Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects* (available at: www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/)

Donoghue T *et al* 2020 Parameterizing neural power spectra into periodic and aperiodic components *Nat. Neurosci.* **23** 1655–65

Erbil N and Ungan P 2007 Changes in the alpha and beta amplitudes of the central EEG during the onset, continuation, and offset of long-duration repetitive hand movements *Brain Res.* **1169** 44–56

Freudenburg Z V *et al* 2019 Sensorimotor ECoG signal features for bci control: a comparison between people with locked-in syndrome and able-bodied controls *Front. Neurosci.* **13** 1058

Graimann B, Huggins J E, Levine S P and Pfurtscheller G 2002 Visualization of significant ERD/ERS patterns in multichannel EEG and ECoG data *Clin. Neurophysiol.* **113** 43–47

Haegens S, Cousijn H, Wallis G, Harrison P J and Nobre A C 2014 Inter- and intra-individual variability in alpha peak frequency *NeuroImage* **92** 46–55

Hayashi H and Kato S 1989 Total manifestations of amyotrophic lateral sclerosis. ALS in the totally locked-in state *J. Neurol. Sci.* **93** 19–35

Höhne J, Holz E, Staiger-Sälzer P, Müller K-R, Kübler A and Tangermann M 2014 Motor imagery for severely motor-impaired patients: evidence for brain-computer interfacing as superior control solution *PLoS One* **9** e104854

Hotz M A, Ritz R, Linder L, Scollo-Lavizzari G and Haefeli W E 2000 Auditory and electroencephalographic effects of midazolam and alpha-hydroxy-midazolam in healthy subjects *Br. J. Clin. Pharmacol.* **49** 72–79

Ives-Deliperi V L and Butler J T 2018 Relationship between EEG electrode and functional cortex in the international 10–20 system *J. Clin. Neurophysiol.* **35** 504–9

Kappenman E S and Luck S J 2010 The effects of electrode impedance on data quality and statistical significance in ERP recordings *Psychophysiology* **47** 888–904

Lanfer B, Röer C, Scherg M, Rampp S, Kellinghaus C and Wolters C 2013 Influence of a silastic ECoG grid on EEG/ECoG based source analysis *Brain Topogr.* **26** 212–28

Leinders S, Vansteensel M J, Branco M P, Freudenburg Z V, Pels E G M, Van der Vijgh B, Van Zandvoort M J E, Ramsey N F and Aarnoutse E J 2020 Dorsolateral prefrontal cortex-based control with an implanted brain-computer interface *Sci. Rep.* **10** 15448

Lejko N, Larabi D I, Herrmann C S, Aleman A and Ćurčić-Blake B 2020 Alpha power and functional connectivity in cognitive decline: a systematic review and meta-analysis *J. Alzheimers Dis.* **78** 1047–88

McFarland D J, Miner L A, Vaughan T M and Wolpaw J R 2000 Mu and beta rhythm topographies during motor imagery and actual movements *Brain Topogr.* **12** 177–86

Miller K J, Leuthardt E C, Schalk G, Rao R P N, Anderson N R, Moran D W, Miller J W and Ojemann J G 2007 Spectral changes in cortical surface potentials during motor movement *J. Neurosci.* **27** 2424–32

Milligan K R, Lumsden J, Howard R C, Howe J P and Dundee J W 1989 Use of auditory evoked responses as a measure of recovery from benzodiazepine sedation *J. R. Soc. Med.* **82** 595–7

Mitra P P and Pesaran B 1999 Analysis of dynamic brain imaging data *Biophys. J.* **76** 691–708

Neuper C and Pfurtscheller G 2001a Event-related dynamics of cortical rhythms: frequency-specific features and functional correlates *Int. J. Psychophysiol.* **43** 41–58

Neuper C and Pfurtscheller G 2001b Evidence for distinct beta resonance frequencies in human EEG related to specific sensorimotor cortical areas *Clin. Neurophysiol.* **112** 2084–97

Neuper C, Wörtz M and Pfurtscheller G 2006 ERD/ERS patterns reflecting sensorimotor activation and deactivation *Prog. Brain Res.* **159** 211–22

Nottage J F and Horder J 2015 State-of-the-art analysis of high-frequency (gamma range) electroencephalography in humans *Neuropsychobiology* **72** 219–28

Ogata K, Nakazono H, Uehara T and Tobimatsu S 2019 Prestimulus cortical EEG oscillations can predict the excitability of the primary motor cortex *Brain Stimul.* **12** 1508–16

Ohara S *et al* 2000 Movement-related change of electrocorticographic activity in human supplementary motor area proper *Brain* **123** 1203–15

Oostenveld R, Fries P, Maris E and Schoffelen J-M 2011 FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data *Comput. Intell. Neurosci.* **2011** 156869

Pels E G M, Aarnoutse E J, Leinders S, Freudenburg Z V, Branco M P, van der Vijgh B H, Snijders T J, Denison T, Vansteensel M J and Ramsey N F 2019 Stability of a chronic implanted brain-computer interface in late-stage amyotrophic lateral sclerosis *Clin. Neurophysiol.* **130** 1798–803

Pfurtscheller G and Lopes da Silva F H 1999 Event-related EEG/MEG synchronization and desynchronization: basic principles *Clin. Neurophysiol.* **110** 1842–57

Rogasch N C, Daskalakis Z J and Fitzgerald P B 2013 Mechanisms underlying long-interval cortical inhibition in the human motor cortex: a TMS-EEG study *J. Neurophysiol.* **109** 89–98

Sannelli C, Vidaurre C, Müller K-R and Blankertz B 2019 A large scale screening study with a SMR-based BCI: categorization of BCI users and differences in their SMR activity *PLoS One* **14** e0207351

Stancák A and Pfurtscheller G 1996 Event-related desynchronisation of central beta-rhythms during brisk and slow self-paced finger movements of dominant and nondominant hand *Cogn. Brain Res.* **4** 171–83

van Albada S J and Robinson P A 2013 Relationships between electroencephalographic spectral peaks across frequency bands *Front. Hum. Neurosci.* **7** 56

van den Boom M, Miller K J, Gregg N M, Ojeda Valencia G, Lee K H, Richner T J, Ramsey N F, Worrell G A and Hermes D 2021 Typical somatomotor physiology of the hand is preserved in a patient with an amputated arm: an ECoG case study *Neuroimage Clin.* **31** 102728

Vansteensel M J *et al* 2016 Fully implanted brain-computer interface in a locked-in patient with ALS *N Engl J Med* **375** 2060–6

Veselis R A, Reinsel R, Alagesan R, Heino R and Bedford R F 1991 The EEG as a monitor of midazolam amnesia: changes in power and topography as a function of amnesic state *Anesthesiology* **74** 866–74

von Ellenrieder N, Beltrachini L, Muravchik C H and Gotman J 2014 Extent of cortical generators visible on the scalp: effect of a subdural grid *NeuroImage* **101** 787–95

Wang Y, Hong B, Gao X and Gao S 2006 Phase synchrony measurement in motor cortex for classifying single-trial EEG during motor imagery *Int. Conf. IEEE Engineering in Medicine and Biology Society* pp 75–78

Zhang R, Li F, Zhang T, Yao D and Xu P 2020 Subject inefficiency phenomenon of motor imagery brain-computer interface: influence factors and potential solutions *Brain Sci.* **6** 224–41