Towards calibration-less BCI-based rehabilitation

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***Abstract*—Brain-computer interfaces (BCIs) are increasingly deployed in stroke rehabilitation. Most BCIs rely on batch, supervised parameter estimation which requires large, labelled brain data associated with the motor tasks to be performed during the therapy. Consequently, BCI-based rehabilitation regimes include an initial calibration session aimed at collecting the necessary data to train the BCI model. This calibration process is time-consuming and tedious, especially considering the strict logistical constraints in a clinical setting. This paper investigates the possibility of calibration-free BCI regimes rendering re-calibration sessions entirely redundant. We compare the decoding performance of three different approaches to calibration-less BCI, which exploit either the notion of adaptation or the classical results of event-related synchronization/desynchronization, to that of a conventional, calibration-based classification method, on a large dataset of 26 (sub-)acute stroke patients performing 15 therapeutic sessions. Our results show that calibration-less BCI for stroke treatments is not only possible, thus lifting a major practical barrier hindering the translation of this technology to clinics, but may also be superior to the standard, calibration-based methodology in terms of classification accuracy.**

***Index Terms*—brain-computer interface, calibration, stroke rehabilitation, event-related spectral perturbation (ERSP), Mahalanobis distance, adaptation**

I. Introduction

Brain-Computer Interface (BCI) technology has been effectively used to restore motor function in patients with severe motor impairments caused by stroke [1]. It is hypothesized that BCI-based stroke therapies foster beneficial neuroplasticity promoting recovery by reinstating the intention-action-perception loop of natural motor control that has been broken due to the brain lesion. This is achieved as BCI-driven, rich afferent feedback is temporally coupled to the efferent motor commands decoded by the BCI sparking activity-dependent, associative plasticity [2]. In particular, motor rehabilitation for the upper limb has been largely grounded on "rewarding" sound Event-Related Synchronization/Desynchronization (ERD/ERS) modulation of sensorimotor rhythms (SMR) through a wide range of feedback types and end-effectors [2]–[8].

SMR-based BCI conventionally requires a calibration phase before it can decode motor intentions from raw electroencephalography (EEG) signals in real-time [2], [9]. This is due to the usual employment of supervised machine learning methods to learn the parameters of the BCI model, techniques that require labelled, ground truth data. During calibration, the subject is asked to repeatedly rehearse the same motor tasks that will be later exercised and detected by the BCI in the therapeutic sessions, while the examples of the brain activity corresponding to these tasks are recorded and labelled by the experimental protocol. Furthermore, due to the non-stationary nature of brain activity, the performance of trained BCI models may soon degrade, and novel calibration procedures are necessary to reinstate decoding accuracy [10], [11]. Even if re-calibration is grounded on recent "online", closed-loop data derived from the therapeutic sessions, so that additional re-calibration sessions for data collection are not needed, the re-training process is likely to demand the presence of expert, technical personnel, increasing the regime's complexity.

Re-calibration sessions are time-consuming and demotivating for patients, as they do not involve closed-loop control [11]. The need for calibration reduces the therapy's intensity as therapeutic sessions need to be pushed back to interleave calibration ones or classifier re-training. Overall, the calibration stage and/or the re-calibration/re-training procedures pose a severe obstacle considering the stringent logistical and financial constraints in clinics. Therefore, the identification of calibration-free methods is essential for the technology transfer of BCI-based clinical interventions.

The issue of calibration-less ("zero-training") BCI has been studied as one of the main motivations behind the BCI adaptation literature [12]. However, most of these investigations are based on able-bodied users [13]–[16] and primarily regard assistive applications (e.g., there is a focus on unsupervised adaptation [17], largely unnecessary in the rehabilitation context where labels can be available). Very few works have addressed the problem specifically within the BCI-based rehabilitation context, employing either subject-specific adaptation [18] or various forms of transfer learning [19], [20]. Of note, although EEG markers of motor imagery/attempt in stroke patients tend to be similar to those of able-bodied individuals, they are likely to be weaker and less consistent, leading to lower single-trial classification accuracy [2], [21]. Hence, SMR classification in stroke poses greater challenges than in general SMR BCI literature.

Here, we investigate the possibility of calibration-free BCI-based methods for stroke rehabilitation emphasizing the use of algorithms that enable the immediate launch of therapy without imposing any prerequisite. In particular, we wish to discard the need for either previous patient data for adaptation, or subject-unspecific data for transfer learning. We report on a novel dataset of 26 sub-acute stroke patients undergoing 15 therapeutic sessions. We compare the classification accuracy obtained online by the conventional calibration method, to that of three different calibration-less schemes based on i) a supervised adaptive algorithm ii) Event-Related Spectral Perturbation (ERSP) extraction, and iii) Mahalanobis distance of SMR patterns from resting-state distributions. Our findings indicate that calibration-free BCI-based rehabilitation algorithms can be established, discarding calibration needs without compromising performance.

II. Methods

A. Participants

We assessed 26 acute/sub-acute stroke patients with severe hemiplegia (16 male, 62 ± 11 years old) recruited in 5 clinical centres in Germany, Switzerland and Italy. All patients signed informed consent and the study was approved by the local ethical committees. The study was designed as a double-blind, randomized controlled trial. The basic inclusion criteria were first unilateral stroke leading to severe hemiparesis (Medical Research Council (MRC) muscle strength <= 2 points for extensor muscles of the affected hand), and admission maximum 3 months post-stroke. Patients were assigned to two groups, BCI (intervention arm, $N = 13$) and Sham-BCI (control, $N = 13$) using Frane's minimization algorithm for randomized allocation, balancing several identified confounds (gender, age, lesion side, lesion site, etc.).

B. Study and BCI protocols

Each patient underwent 15 therapeutic sessions over 3-5 weeks involving the training of a wrist/palm extension movement, and 3 screening sessions (pre-intervention, post-intervention, and 6-month follow-up) where the motor and resting-state tasks were performed in open-loop with high-density EEG, and clinical assessments were carried out. Here, only the data derived from each participant's 15 therapy sessions are used. The primary outcome was Fugl-Meyer Assessment of the upper limb, with several other clinical scales (e.g., MRC) monitored at the three endpoints.

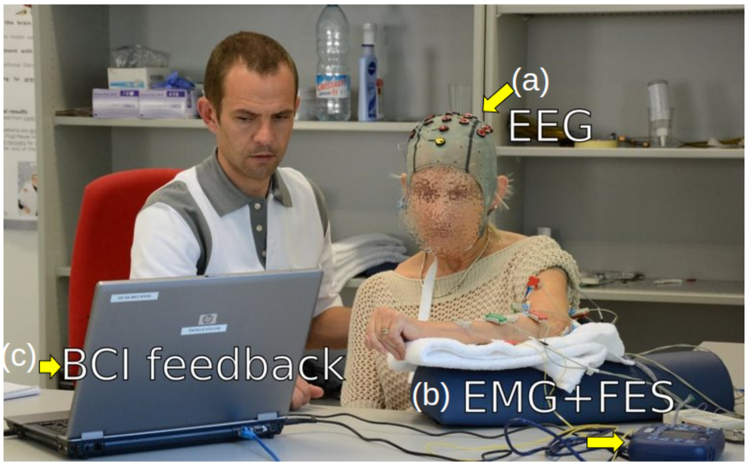
The therapy comprised repetitions of BCI-triggered, Functional Electrical Stimulation (FES)-actuated movements (wrist/palm extension of the affected upper limb by stimulating the *extensor digitorum communis* muscle and nearby muscle sites of the forearm). The EEG and FES (Motionstim 8, Medel, Germany) hardware/software configuration (Fig. 1), the BCI processing, the group design (BCI vs Sham-BCI) and the experimental protocol are also partially reported in [21] and follow closely those described by Biasiucci et al. [2].

Fig. 1a illustrates the experimental setup of a therapeutic session. In these sessions, brain activity was acquired via 16 active EEG channels over the sensorimotor cortex (Fig. 1b): Fz, FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4, CP3, CP1, CPz, CP2, and CP4 according to the international 10-20 system with reference on the right ear and ground on AFz. The EEG was recorded with a g.USBamp system (g.Tec, Austria) at 512 Hz. Raw signals were bandpassed between 0.1 Hz and 100 Hz, and notch-filtered at 50 Hz.

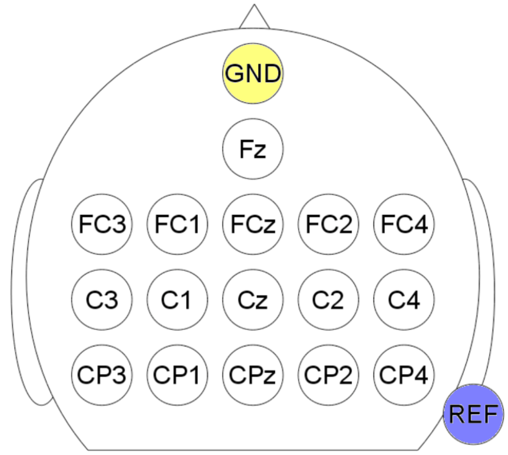
For each trial repetition, patients were requested to perform attempted wrist extension movements of the affected hand [2], [21], whose SMR EEG correlates have been shown to be similar to those elicited during Motor Imagery (MI) (ERD/ERS) [22]. A therapy session included 3-7 runs (blocks) comprising 15 trials each. As shown in Fig. 1c, each trial started with a 2 s "fixation stimulus" epoch, during which patients were instructed to fixate a cross in the middle of the screen and prepare for the upcoming movement attempt, avoiding inducing any artifacts. This was followed by a 1 s "cue" epoch (arrow pointing upwards) instructing the user to commence their motor attempt. In the motor attempt epoch, the BCI was continuously classifying in closed-loop the patient's SMR as either "rest/no-movement" or "motor attempt". Consecutive classification decisions were integrated with an exponential smoothing filter, the output of which was visualised through a grey, "liquid-cursor" bar and fed back to the patient, as in [2], [9]; unlike its predecessor study in chronic stroke [2], in this case, patients were shown visual feedback, as depicted in Fig. 1c. The motor attempt epoch would successfully finish either when the patient was able to produce adequate and timely ERD/ERS in order to push the liquid cursor upwards enough so as to reach a re-configurable (by the therapist) threshold, or when the epoch would time-out (7 s). Only in the former case, reaching the threshold would trigger the FES wrist extension movement and show a trial-end/decision-reached feedback for 1 s. The end of the motor attempt epoch was followed by an inter-trial interval lasting randomly between [3, 4] s, before the next trial takes place.

Before the therapy, a calibration session (3-4 runs) was imposed to collect data for training the BCI classifier. These runs interleaved, in random order, 15 motor attempts with 15 "rest"/no-movement trials, all of which lasted 4 s, with fake/positive feedback. The trial structure and feedback graphics were otherwise identical to those of the therapy runs. Importantly, as the results reported here refer to the online/therapy runs only, the fixation-cross epoch is used to derive instances of "rest"/"no-move" data.

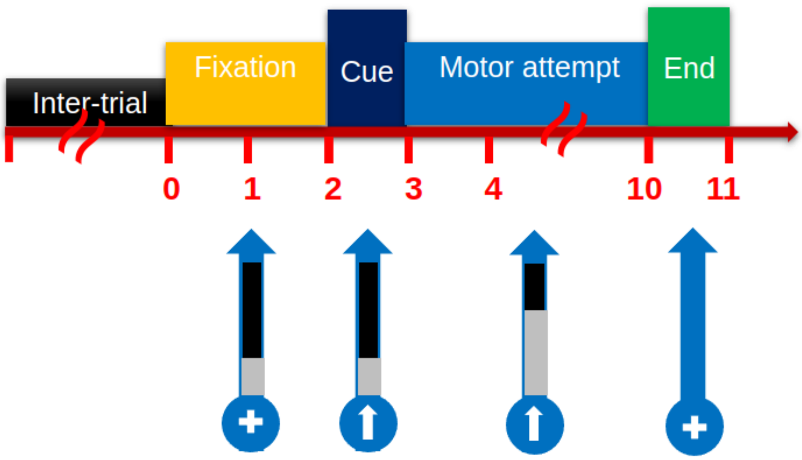
A new BCI decoder was manually produced every week using data from the preceding week's therapeutic sessions so that our calibration-based benchmark already reflects a mild ("offline", periodic, subject-specific) adaptation. Of note, re-calibration was always performed by the same BCI expert and extended to Sham participants (for effective blinding). Participants in both groups underwent the exact same protocol, wearing the same apparatus; the only difference is that, in the Sham-BCI group, FES-based movement execution is triggered at random, and does not depend on the patient's SMR modulation. This was achieved by "playing back", for each participant in the Sham group, the EEG data of a matched patient in the BCI group.



(a) Experimental setup of therapy sessions.



(b) EEG placement.



(c) Trial timeline of a therapeutic run.

Fig. 1: Experimental and protocol setup.

C. EEG processing, feature extraction and selection

EEG channels are spatially filtered with a cross-Laplacian derivation, where the uniformly weighted sum of the orthogonal neighbouring channels is subtracted from each channel. The Power Spectral Density (PSD) of each Laplacian channel was estimated during the movement attempt or no-movement period for the frequency bands 4 to 48 Hz with 2 Hz resolution (23 bands) in sliding 1 s windows shifting by 62.5 ms with the Welch method and identical parameterization to [2]. For the actual therapy sessions, the most discriminant EEG spatio-spectral features were selected to build the BCI classifier as in [2], [23], [24].

For the calibration-less methods introduced here, to eliminate the supervised feature selection procedure that is part of conventional calibration and alleviate overfitting, we reduce the feature vectors to 24 PSD features by considering only 12 lateral channels–FC3, FC1, FC2, FC4, C3, C1, C2, C4, CP3, CP1, CP2, and CP4–and 2 broad–averaging the original feature space–frequency bands: μ (8-14 Hz) and β (18-24 Hz).

D. Calibration-based and calibration-free methods

We compare three calibration-less schemes to the calibration-based approach that was actually used during online BCI operation at the therapeutic sessions. The calibration-free methods concern i) a supervised adaptive algorithm relying on Quadratic Discriminant Analysis (QDA) ii) extraction and thresholding of ERSP, and iii) Mahalanobis distance of SMR patterns from resting-state distributions. The following sections describe each of these algorithms in greater detail.

E. Calibration-based classification

The calibration-based method is the one presented in [2]. PSD feature vectors were classified with a Gaussian mixture model (GMM) framework [24]. For each incoming PSD sample at time t, the output of the GMM resulted in a posterior probability distribution over the two mental classes c (motor attempt "move", resting "no-move") $p_t(c|\mathbf{x_t})$ =

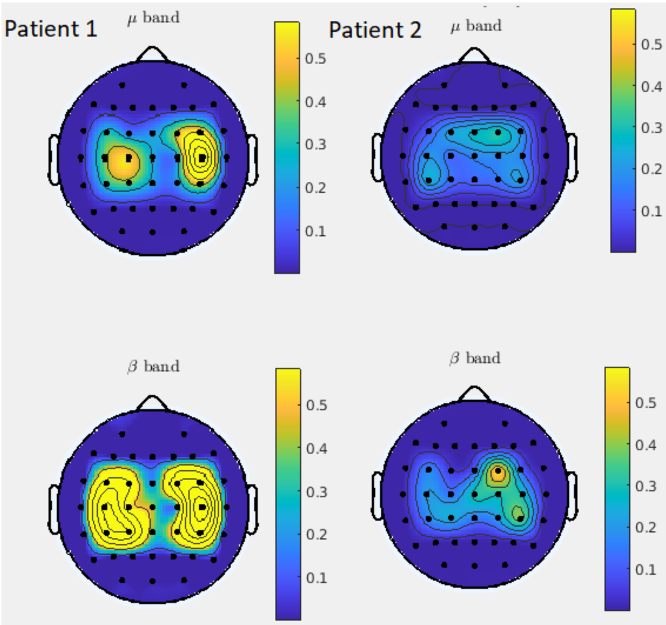


Fig. 2: Exemplary topographical SMR distribution for two patients with strong (left) and weaker (right) ERD/ERS.

$[p_t^{move}, p_t^{no-move}]$. Each mental class is represented by 4 Gaussian units. Uniform priors for the classes and mixture coefficients are assumed, as well as shared, diagonal covariance matrices. The centroids of the Gaussian units are initialized by means of self-organizing map clustering and their covariance matrices are subsequently computed as the pooled covariance matrices of the data closest to each prototype. Finally, the distribution parameters are, iteratively re-estimated through gradient descent so as to reduce the mean square error (MSE) [25]. The training of the Gaussian classifier stops, if the MSE change after each iteration is not improving, or after 20 iterations at maximum [24], [25]. As already described, during the actual therapy, posteriors $p_t(c|\mathbf{x_t})$ were further processed with an evidence accumulation framework (exponential smoothing) to drive the feedback and the FES; for the purposes of this work, each sample $\mathbf{x_t}$ is classified as belonging to the mental class with the highest posterior probability, in order to extract classification accuracy.

F. Supervised adaptive QDA

Online parameter estimation of the BCI model discards the need for re-calibration sessions and presents what is probably the most straightforward avenue towards calibration-less BCI-based rehabilitation. Since in the context of a rehabilitation protocol motor tasks are instructed and not self-paced, BCI adaptation can proceed in a supervised manner, which simplifies the algorithmic design and guarantees convergence properties [11], [17]. To represent the BCI adaptation approach in our comparison, we here devise an adaptive method based on QDA.

Specifically, we accumulate the latest available 2000 PSD samples $\mathbf{x_t}$ derived by elapsed motor attempt ("move") and fixation ("no-move") epochs in the ongoing and previous runs of a participant's data. $\mathbf{x_t}$ regards the 24 broad-band, lateral feature vectors employed also for the other calibration-less methods. The classifier is updated during the inter-trial interval every time 3 new trials are completed. The update consists in selecting the 5 (out of 24) best features according to r^2 separability and subsequently computing on these further reduced space $\mathbf{x_t'}$ the mental class-specific mean vectors/centroids $\mu_\mathbf{c}$ and full covariance matrices Σ_c (with Oracle Approximating Shrinkage [26] to counteract overfitting, especially while the adaptation buffer is mostly empty at the beginning of adaptive learning). Effectively, a multivariate normal distribution $N_c(\mu_\mathbf{c}, \Sigma_c)$ is fitted to the data of each class ("move", "no-move"), which constitutes the generative dual of a QDA classifier. Similarly to the calibration-based approach (see Section II-E, posteriors $p_t(c|\mathbf{x_t'}, \mu_\mathbf{c}, \Sigma_c)$ are derived at each time t, and the class exceeding a probability of 0.5 "wins" the corresponding sample. The PSD samples of the first 3 trials of the simulation where no adaptive classifier exists are excluded from the calculation of classification accuracy.

G. ERSP-based movement detection

ERD/ERS refers to brain oscillatory activity responses in specific frequency bands and cortical locations that are widely used in SMR BCI. Strong ERD/ERS activation during motor tasks is distinguishable from the "resting" state and even distinct of the particular motor action performed [22]. ERSP refers to numerically stable approaches to quantify ERD/ERS phenomena describing the relative change in the EEG power following some endogenous motor task and reflecting a measure of the deviation of the bandpower relative to a baseline period. Here, we adapt an ERSP definition as:

$$ERSP_t^f = \frac{|x_t^f - \mu_{no-move}^f|}{s_{no-move}^f} \tag{1}$$

where $\mu_{no-move}^f$, $s_{no-move}^f$ are the mean and standard deviation of the PSD feature f (for all f among the aforementioned 24 features) retrieved in the preceding fixation epoch of the motor attempt trial where sample $\mathbf{x_t}$ belongs. Effectively, $ERSP_t^f$ represents the z-score of motor attempt samples with respect to the most recent estimate of the "rest" distribution for a particular spatio-spectral feature [27]. This metric relies on the notion that motor attempt periods should generate large z-score values, well outside high-density PSD value area of the no-movement distributions.

As $ERSP_t^f$ is a univariate metric calculated individually for each feature f, we examine 3 variants of decision making taking into account the evidence by all features: either thresholding the–across features–average or the maximum, or individually thresholding features and produce a final "move vs no-move" decision through majority voting.

H. Mahalanobis distance movement detection

The third calibration-less approach tested resides on the same idea, but directly derives a multivariate metric to quantify the deviation of a sample $\mathbf{x_t}$ from the "resting

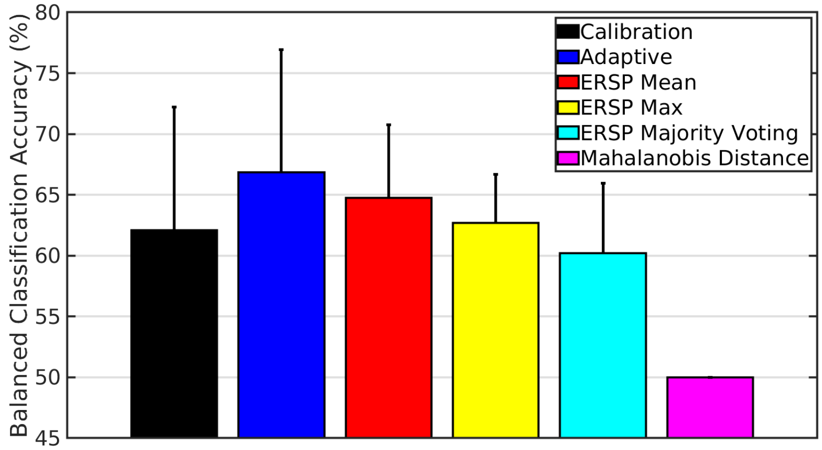


Fig. 3: Average and standard deviation of balanced accuracy for all methods.

state" through the sample's Mahalanobis distance [28] $D(\mathbf{x_t})$ from the (covariance-shrinked) multivariate normal distribution $N(\mu_{no-move}, \Sigma_{no-move})$ of the preceding fixation epoch, which is subsequently thresholded:

$$D(\mathbf{x_t}) = \sqrt{(\mathbf{x_t} - \mu_{no-move})^T * \Sigma_{no-move}^{-1} * (\mathbf{x_t} - \mu_{no-move})} \quad (2)$$

III. Results

Fig. 2 represents the average Fisher Score separability of PSD samples between the move and no-move mental classes in the μ (8-14 Hz) and β (16-24 Hz) bands for the two patients exhibiting the highest (left) and lowest (right) classification accuracy with the calibration-based approach actually used during the therapy. It provides favourable evidence for the soundness of the motor tasks performed by patients in the study. Specifically, both patients showcase prominent SMR modulation in the anticipated μ and β bands, which is lateralized (mostly contra-lateral–the affected hand is the right hand for Patient 1 ad the left one for Patient 2–but, also with a strong ipsilateral component, especially for Patient 1), as expected for regular motor EEG correlates. Furthermore, the magnitude of SMR separability is consistent with the classification accuracy obtained for these two patients, where high accuracy is accompanied by neurophysiologically relevant SMR patterns of activity, similar to those manifesting in able-bodied and/or spinal cord injury BCI users performing motor imagery [9], [17].

With regard to the comparison among calibration-based and calibration-free methods, in order to account for the class imbalance between motor attempt and no-movement intervals in terms of the number of samples available in each category in our dataset, we report "balanced" classification accuracy (average of the true positive and true negative rates of the obtained confusion matrix for each patient and algorithm). For each method, we provide results for a single, optimized threshold applied to all subjects and sessions, so that the proposed methods involve no learning of (hyper)-parameters other than what can be seamlessly computed in a standard protocol.

Fig. 3 presents the average, method-wise balanced classification accuracy across patients. Evidently, the calibration-free algorithms proposed here are competitive to a standard, calibration-based approach. Specifically, the adaptive algorithm is significantly superior ($p = 0.005$) and the ERSP-Mean marginally so ($p = 0.07$, paired, two-sided t-test). The Mahalanobis distance method did not perform better than a random classifier due to intense overfitting, in spite of using covariance shrinkage for regularization; however, the successful application of univariate ERSP, which shares the same underlying idea, suggests that it could work with a reduced feature space and/or longer resting epochs.

IV. Discussion

Our results strongly indicate that a calibration phase for supervised training of SMR BCI classification models, currently the method-of-choice (also) in stroke rehabilitation protocols despite the logistic concerns raised, is not really necessary. Adaptive classification with virtually "zero" calibration needs (i.e., in this work, only 3 trials are needed to output the first classifier; fake or no feedback provided for this short interval should be acceptable in the rehabilitation setting) is shown to significantly outperform, on average, the standard, calibration-based BCI. Importantly, methods based on simple ERSP-inspired movement intent detection from EEG are also competitive to the supervised classification model; this is a critical observation, as there can be occasions or individuals (e.g., increased artifact production due to concomitant deficits for certain stroke patients, such as spasticity or dyskinesia) where adaptive approaches may be ill-advised, due to their vulnerability of adapting to noise.

Our findings substantiate the claim that the calibration stage in BCI-based rehabilitation regimes, where the natural availability of labels and the seamless incorporation of short resting-state epochs allow for supervised adaptation and ERD/ERS-inspired methodologies, can be spared without detriment. This conclusion yields considerable impact on the design and logistics of BCI-based rehabilitation interventions. Furthermore, our findings have good potential and can be applied to other BCI-based motor rehabilitation regimes (e.g., for spinal cord injury patients). Our future work will focus on fine-tuning these approaches and extending their evaluation to bigger datasets.

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