Tracking Event-Related Potentials during BMI driven Rehabilitation

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Abstract— **Current brain-machine-interface (BMI) rehabilitation approaches typically focus on a specific aspect of neural activity. Auxiliary signals, derived from independent measures of neural activity and recorded in parallel might be useful in quantifying and tracking a subjects mental state and performance. In this work, we demonstrate that event-related potentials can be reliably observed in stroke survivors with chronic paralysis during a BMI intervention. The averaged evoked response remains stable over sessions and varies between subjects. A prominent negativity, positivity complex emerges whose features can be tracked across subjects and sessions.**

I. INTRODUCTION

Over the course of the past decades Brain-machine-interface (BMI) driven rehabilitation therapies have been developed to address the lack of proper therapeutic interventions for chronic paralysis after stroke. Such systems estimate the neuronal activity of their users (patients) by various techniques (e.g. electro- or magneto-encephalography, electrocorticography, microelectrode recordings, near-infrared spectroscopy etc.) to derive markers of movement intention and/or cortical pre-motor activation and provide coherent visuoperceptive feedback to the users by means of electrical stimulation or robotic actuation of their paretic limbs. The efficacy of the general concept has been demonstrated [1] and confirmed [2], [9], [7], [12].

However, while the method has been proven to be efficient on the population level it features a high inter-subject variability. Individual subjects will respond to the training with individual progress and success which spans from appreciable to zero improvements. It remains unclear to what extend the observed differences can be attributed to physiological or functional dissimilarities. Concordantly it remains unexplored whether or not such dissimilarities can be compensated for by the therapeutic system yielding an optimal therapy for all subjects.

Meanwhile current BMI rehabilitation approaches typically focus on a specific aspect of neural activity (i.e. event-related desynchronization in the case of motor imagery BMIs). To ensure that the chosen aspect is present in the data, let it be a certain channel or an aggregate of multiple channels, the systems tend to record much more data than they need to drive the actual control. Various aspects of neurophysiological data in the time and frequency domain are known to capture a plethora of behavioral neural correlates [5], [4] , but it remains unclear to what extent the information present in such auxiliary signals can be used to track and aid the progress of a subject performing in BMI rehabilitation.

In this study we pose the question whether it is possible to track a secondary neurophysiological marker (of sensory processes i.e. features of auditory event related potentials) over the course of an BMI interventional study in which the subjects primarily train a different neurophysiological marker (i.e. desynchronization of the sensory-motor rhythm). With this we hope to establish the foundation for nested loop BMI interventions in which the secondary marker is used to drive the adaptation of the BMI system towards individualized and optimized therapeutic efficacy.

II. METHODS

A. Participants and Paradigm

This work is built upon data acquired during a previous study with 32 stroke survivors suffering from chronic paralysis of the arm and hand (cFMA 12 ± 9) undergoing either BMI or sham-BMI training. Over the course of 2-4 weeks of training each participant performed between 250 and 300 runs, each run consisting of 11 trials. In each trial, the subjects were provided with an auditory instruction/priming cue followed two seconds later by a imperative/go cue, the latter being coincident with the start of a 5 second BMI feedback period. During this period the subjects controlled a robotic orthosis with the relative desynchronization of their ipsilesional rolandic (sensorimotor rhythm [SMR]) brain oscillations. The trials were separated by an 8 seconds relaxation interval. For further details on the subject population, demographics and intervention design we refer to the original works [11], [1].

B. Data Processing

Data processing was performed adhering to the guidelines provided in [8], [14]. The raw data was zero-phase bandpass filtered between 0.1 - 40 Hz with a transition band of 0.25 around the respective band-edge frequencies. All EEG channels were re-referenced to their common average (CAR). Epochs spanning 2 s before and 3 s after stimulus onset were extracted and baseline corrected using the pre-stimulus time. Traces of Cz were selected for further analysis. Epochs that showed EEG fluctuations larger than 100uVp-p were rejected (approx. 10% of trials). Evoked potentials were calculated as the arithmetic means of Epochs for each subject

This work was funded by the fortuene-Program of the University of Tuebingen (2422-0-1 and 2452-0-0), the Bundesministerium fuer Bildung und Forschung BMBF MOTORBIC (FKZ 13GW0053) and AMORSA (FKZ 16SV7754) and the Deutsche Forschungsgemeinschaft (DFG)

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and session. Aligned correlation coefficients were calculated as the maximum of delayed correlations between evoked potentials. Waveform metrics were extracted as indicated in 5.

III. RESULTS

A. Single Session

In figure 1A the epochs of the central electrode Cz of a single session and subject are displayed as a color matrix in which rows represent individual epochs, columns represent time points and pixel color signals voltage value. The coherent coloring across columns indicates time-locked activity, which is summarized in the arithmetic mean across epochs shown in 1B. Gray shading marks the 95% confidence interval obtained by bootstrapping. In the long-term display, a three-phase picture typical for most subjects emerges: (1) about 300ms after cue onset an event-related potential complex emerges from the noise background. (2) It follows a 2 seconds interval of slight negativity (baseline or positivity in some subjects). (3) After 2.5s a second potential complex can be observed. The short-term dynamics of the first potential complex (PCo1) shown in figure 1C reveal a smaller negative potential peaking about 350ms after stimulus onset followed by a larger positivity peaking at 425ms.

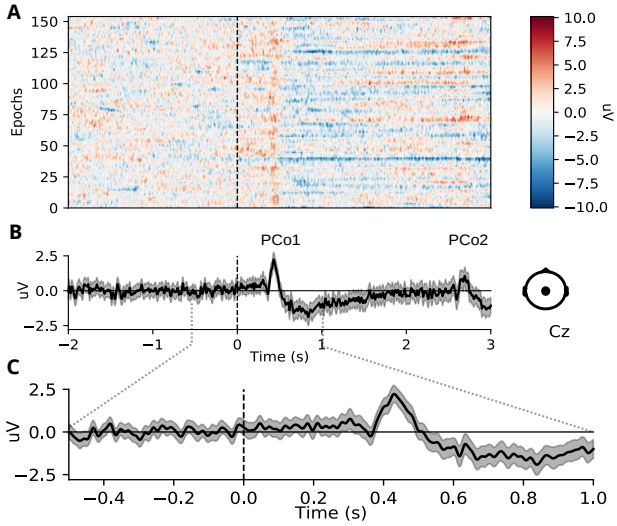

Fig. 1. Epochs and average of a single session. **A**: Individual epochs shown as rows, color representing voltage. **B**: Average of epochs (black) with 0.95 confidence interval (gray). **C**: Zoom on the average potential around first cue onset.

The full topography of the primary potential complex is shown in figure2. Electrode configuration and the setups focus on central electrode signal quality leads to a somewhat limited topographic mapping of the event-related potential components. Never the less an initial negativity between central and parietal electrodes emerges about 325ms containing the negative peak on Cz, followed by a bilateral temporalization of the potential peaking at about 425ms and leaving Cz as saddle-node between temporal-parietal negativities and frontal positivity. About 600ms post-stimulus the potential topography equalizes and continues to invert its orientation to a lower amplitude frontal negativity with parietal positivity beyond 800ms.

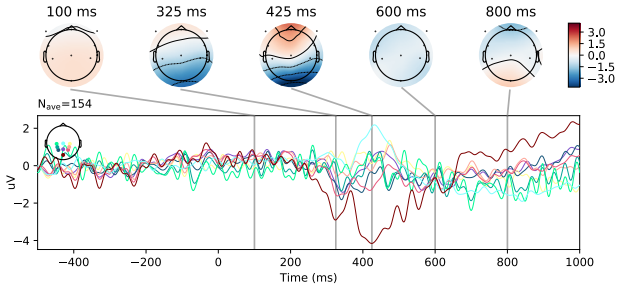

Fig. 2. The topography of evoked potentials. Instantaneous potential distributions are shown for multiple post stimulus time-points, marked in the electrode traces plotted below. The spatial color coding of electrode traces is shown in the head-pictogram (top left corner of the box).

B. Across Sessions

Averaging over the epochs of individual sessions yields approximations of the evoked potential for the respective session (3). The rows of traces were derived from successive training sessions from first (top) to last (bottom). Stereotypic waveforms are observable for a single subject across sessions. The negativity and positivity described before can be identified in almost all sessions for both subjects. While the general shape of the waveform is consistent over sessions, amplitude and timing are not. The property of (linear) shape similarity is quantified in figure 4 and also compared across subjects.

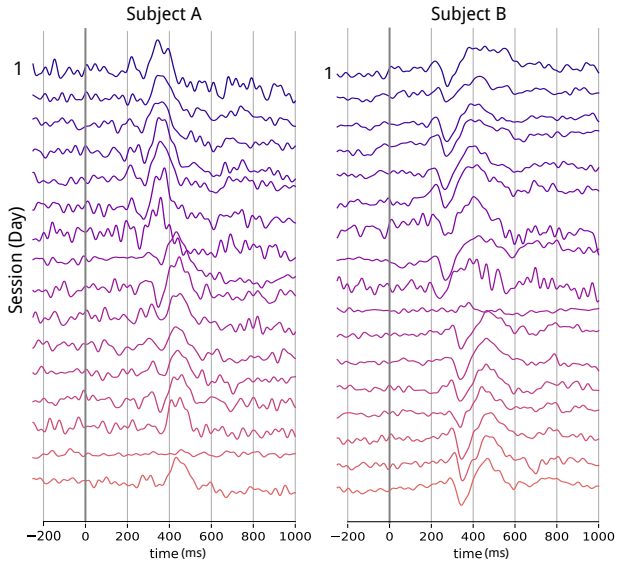

Fig. 3. Evoked potentials across sessions. Averaged epochs over one session yield one trace, successive sessions are shown as rows starting with the first training session on the top.

C. Across Subjects

The two subjects shown in figure 3 feature similar waveforms featuring both a negativity, positivity and a subsequent downward slope. Comparable patterns on electrode Cz were only observable in 19 of the 32 subjects under investigation. Quantification of the degree of (linear) similarity between waveforms of subjects and sessions is shown in figure 4. The relative correlation coefficient of aligned waveforms is highest between sessions of a single subject ($\approx$ 0.9) visible as four blocks on the diagonal of the matrix. The similarity between the waveforms of different subjects is lower (≈ 0.75) but still profound.

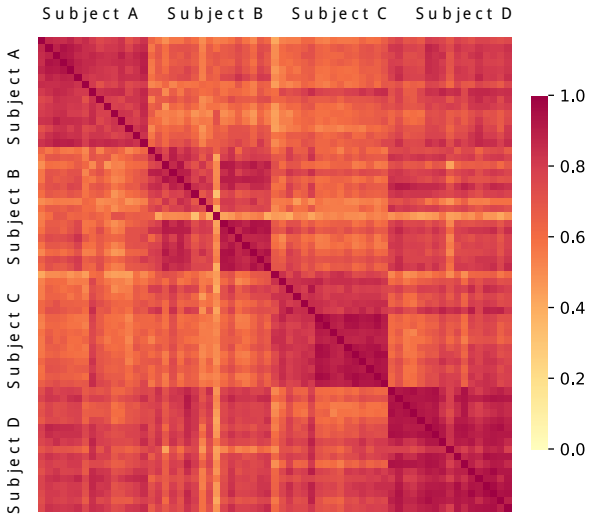

Fig. 4. Aligned correlation matrix of evoked responses. Each entry of the matrix is the maximum over delayed correlations of each session's evoked response. Values range between 1 (similarity) to 0 (independence). Rows and columns correspond to the individual sessions of all subjects.

D. Tracking ERP Metrics

Relative and absolute amplitude and delay metrics were extracted from the session-wise ERP waveforms as shown in figure 5A. Regression analysis for each subject shows that the data does not support a linear relationship between any of the metrics and the training sessions (small adjusted R^2 and p values above 0.1 in figure 5B).

IV. DISCUSSION

A. Identifying ERPs During Convoluted Tasks

The paradigms performed by the subjects over the course of a BMI rehabilitation analyzed in this work are quite different from those used in classical ERP experiments. While the general structure of "instruction/ready" and "go" cues followed by active or passive movements remains comparable to regular paradigms the fast succession of tasks, the complex and long stimuli and the relationship between stimuli delivery and task demands are very different from typical paradigms, in which the sensory input modality is well defined (e.g. auditive or visual) and the output is limited

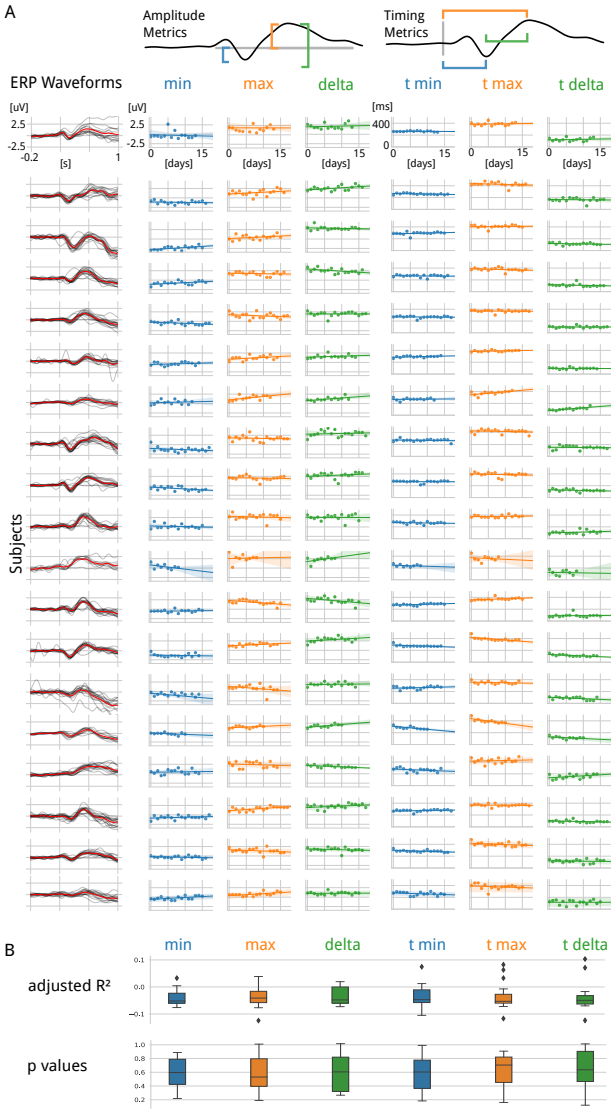

Fig. 5. Measures of PCo1 for all subjects along sessions.**A**: Description of the extracted metrics (top), evoked waveforms and average for individual subjects (left) and time-course of the described markers over sessions superimposed with regression fits and bootstrapped 95% confidence intervals (center). **B**: Summary of the regressions adjusted R values and p values for the associated F-statistic.

to a specific muscle contraction (i.e. pressing a button). The convoluted nature of the task-setup presented here can be described along figure 1B. The first consistently observable fluctuation seen in our data is PCo1 consisting of a negativity and subsequent positivity starting 325 ms after stimulus onset in some subject preceded by another positivity. The timing matches that of an N2/P3 like event. However, P3 is typically described as part of an orienting response towards novel stimuli in the framework of context updates [6] and vanishes when novelty is missing, while our paradigm doesn't feature any novel stimuli but a fixed sequence known to the subject. Judging from the order of appearance and topography the potentials might also be identified with a very delayed N1/P2 vertex potential [8], [10], whose delay might be a consequence of the relatively long stimulus (full verbal

phrase) and less controlled delivery (technical delay). The second potential complex (PCo2) that is visible in the long-term evoked response coincides with the delivery of the "go"-cue and constitutes an independent second auditory ERP, possibly in superposition with the late Bereitschaftspotential (late BP) of movement planning and initiation as well as the motor-potential (MP) of movement execution [13]. Between both complexes, a slight negativity is observed that one might identify with a contingent negative variation (CNV) described in classical two-stimulus configurations [8]. The slow components of PCo2 and following potentials have been analyzed in detail in preceding work [15], in which the authors observed prolonged late BP/MP activity in stroke survivors when they attempted movements with their healthy limb compared to their impaired limb.

B. Stability of the ERP Complex PCo1

Complementary to prior work we focus our analysis on the other reliably observable complex PCo1, which shows stability in terms of waveform shape across sessions and to some extent across subjects (see figures 3 and 4). Individual differences in ERP component composition, timing and topography are well known in the literature, sometimes called ERP finger-prints. They are found to be a consequence of (1) the unique arrangement cortical neuron orientation in gyri and sulci that yield unique dipole-moment configurations when simultaneously active and (2) individual differences in those synchronized activation dynamics which combine to become manifest in an individual time-course and topography of the potentials on the skull as measured by EEG [8]. In the case of stroke survivors, the lesioned section of the cortex and/or subcortical structures further individualizes the observed ERPs. Either through the distortion of the dipole moments through passive e.g volume conduction effects or through the alteration of neuronal activation patterns on the functional level. Despite individual differences, the positive potential can be observed in all, the negative in most subjects that show any consistent ERP on Cz.

C. Tracking PCo1 Amplitudes and Latencies

To demonstrate that tracking of ERP components is feasible across sessions and subjects we extracted six absolute and relative metrics (peak-amplitudes and peak-times and their differences) from the from PCo1 components and observed their behavior over training sessions. Linear trends on a by-subject basis are not supported by the data as documented by regression analysis (figure 5B), which indicates that any processes associated with the observed potentials are not subject to long-term changes over the course of the BMI intervention. This finding is to some extent complementary to the results of recent analysis on the same data that revealed long-term changes in the primary EEG marker used to control the BMI, sensory-motor rhythm desynchronization (SMRD)[Ray et al. in Review]. This puts the observed ERP components in a somewhat orthogonal position to the SMR, further supporting their identification with N1/P2 stimuli processing correlates. Following this interpretation, any changes in potential metrics are expected to happen on the single trial level [8] rather than over the course of the full training. In Future work, the waveforms derived for each subject (fig. 5A left) can be used to derive optimal filters that might enable "online" single trial analysis (and possibly online manipulation) of the PCo1 metrics.

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