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Brain Biomarkers of Motor Adaptation Using Phase Synchronization

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Abstract— **A growing number of brain monitoring tools for medical and biomedical applications such as surgery have been developed. Although many assistive technologies (e.g., brain computer interface (BCI) systems) aiming to restore cognitive-motor deficits are under development, no functional neural indicator or brain biomarker able to track the cortical dynamics of the brain when interacting with new tools and/or novel environments in ecological situations are available. Therefore this study aimed to investigate potential biomarkers reflecting the dynamic cognitive-motor states of subjects who had to learn a new tool. These biomarkers were derived from phase synchronization measures of electroencephalographic (EEG) signals (coherence, phase locking value (PLV)). The findings indicate a linear decrease of phase synchronization for both movement planning and execution as subjects adapt during tool learning. These changes were correlated with enhanced kinematics as the task progressed. These non-invasive biomarkers may play a role in bioengineering applications and particularly in BCI systems, allowing the establishment of co-adaptation/cooperation between the user's brain and the decoding algorithm to design adaptive neuroprostheses.**

I. Introduction

In many medical and biomedical fields, brain monitoring tools are being developed to identify specific neurological events and predict outcomes. Although many assistive technologies aiming to restore cognitive-motor function (e.g., smart neuroprosthetics for disabled populations) are currently underway, few monitoring tools related to sensorimotor integration have been developed. Specifically, such monitoring tools need to uncover new functional neural indicators, or brain biomarkers, that are able to track brain dynamics in ecological situations where humans have to learn to interact with new tools and/or changing environments. Ideally, they should be non-invasive, simple to record and analyze, simultaneously robust and sensitive to changes in brain function in natural situations. However, until now, most investigations aiming to identify brain biomarkers have mainly focused on structural features related to brain disorders (e.g., genetic aspects) [1]. Although helpful, these approaches are not suitable to provide direct indicators to assess the functional status of the brain [1]. Such assessment requires recording the dynamic brain activity with a high (e.g. millisecond) temporal resolution as is done with EEG. Except for some studies [2,3] that suggested that the spectral power computed from the low theta and the alpha bands could be used as a good neural indicator of the adaptation of a new tool, no functional biomarker of cognitive states during sensorimotor learning is currently available. Moreover, these biomarkers [3] do not account for potential functional importance of cooperative brain processes that may be essential to cortical dynamic organization during sensorimotor learning [4,5]. Therefore, we aimed to investigate the existence of brain biomarkers derived from EEG phase synchronization during sensorimotor adaptation to a new tool.

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II. Methods

A. Participants and Apparatus

Ten right-handed healthy adults participated in the study after giving informed consent. All had normal or corrected-to-normal vision. Subjects sat at a table facing a computer screen and, with their right hand, had to perform "center-out" drawing movements on a digitizing tablet linking a central target to one of four peripheral targets. Movement paths were displayed on the screen but the vision of the limb was occluded by a horizontal board. EEG signals were acquired using an EEG cap with 64 tin electrodes which was fitted to the participants' heads in accordance with the standards of the extended International 10-20 system.

B. Experimental Procedure

First, the subjects performed 20 practice trials at the beginning of the experiment in order to be familiarized with the experimental setup. After this familiarization period, the experiment was divided into three sessions: i) pre-exposure, ii) exposure and iii) post-exposure. During the pre- and post-exposure phases, the subjects performed, under normal visual conditions, 20 trials (i.e. 1 block). During the exposure phase (180 trials, i.e. 20 trials x 9 blocks), the subjects had to adapt to a 60º counter clockwise screen cursor rotation. Movements were self-initiated and targets were self-selected one at a time. All the targets were displayed throughout each trial. Subjects were asked to draw a line as straight and as fast as possible to reach the peripheral target from the home target. They were also asked

to avoid following any regular sequence in selecting targets. Unknown to the participants, a trial was aborted and restarted if the time between entering the home target and movement onset was less than 2s. Therefore, participants had enough time to both select the target and plan their movement thus providing an extended time-window to analyze cortical activations related to planning and preparation processes of the motion.

C. Movement Kinematics Analysis

The 2D position of the pen was low-pass filtered using a 5-Hz, eighth-order Butterworth filter. In order to quantify motor performance during both movement planning and movement execution periods, Movement Time (MT) and Movement Length (ML) were computed. MT was defined as the elapsed time between leaving the home circle and entering the target. ML was defined as the distance produced for each trial. For the nine learning blocks, the mean and standard deviation of the ML and MT were computed. In order to take into account any differences in subjects' performance during the pre-exposure phase (i.e., baseline condition) and to focus on changes due solely to adaptation, the MT and ML values were standardized with respect to the pre-exposure stage according to the following equation:

$$SP_i = \frac{P_i - \overline{P_{\mathrm{Pr}\_Exp}}}{SDP_{\mathrm{Pr}\_Exp}} \quad (1)$$

where P_i (P: Parameter) is the value of the kinematic parameter (i.e., MT or ML) computed for the i^{th} single trial performed during exposure, and $\overline{P_{\mathrm{Pr}\_Exp}}$ and SDP_{Pr_Exp} represent respectively the mean and standard deviation across trials of the same parameter computed during the pre-exposure block. The SP_i (SP: Standardized Parameter) values were then averaged across blocks and subjects. These average MT and ML standardized values were statistically tested using a *Wilcoxon signed rank test* to assess any changes between the early and late adaptation phases.

D. EEG Pre-processing

Continuous EEG data were epoched in 2-s windows centered at movement onset. The time-windows before (i.e., planning) and after movement onset were considered. Single-trial data were detrended to remove DC amplifier drift, low-pass filtered to suppress line noise, and baseline-corrected by averaging the mean potential from -1 to 1 s.

E. Phase Synchronization Computation

Generally, the literature focusing on EEG signal analysis compute the synchronization between two time signals $x_i(t)$ and $x_j(t)$ using classical coherence $C_{ij}(f)$ according to the following equation:

$$C_{ij}(f) = \left| \frac{S_{ij}(f)}{\sqrt{S_{ii}(f) S_{jj}(f)}} \right| \quad (2)$$

Where $S_{ij}(f)$ is the cross-spectrum of the two time signals $x_i(t)$ and $x_j(t)$ recorded from two electrodes i and j. Although this measure is classically used in the EEG literature it has been shown that this approach does not separate the effects of amplitude and phase in the relationship between two signals [6]. Therefore, although we used this method, we also computed another measure for assessing the synchrony between two signals named the Phase Locking Value (PLV) [6]. It is defined by only considering the phases of the two signals.

$$\mathrm{PLV} = \left| \left\langle e^{j\Delta\varphi} \right\rangle \right| \quad (3)$$

where $\Delta\varphi$ denotes the phase difference between the two signals (i.e., $\Delta\varphi = \varphi_i - \varphi_j$). The symbol $\langle\ \rangle$ represents the averaging operator (for more details see [6]). Although a complex Gabor wavelet can be used, we computed the phase value using the Hilbert transform defined by equation (4). It must be noted that these two methods provide very similar results when applied to EEG data [7].

$$\tilde{x}_i(t) = \frac{1}{\pi} PV \int_{-\infty}^{+\infty} \frac{x_i(t)}{t - \tau} d\tau \quad (4)$$

In this definition $\tilde{x}_i(t)$ is the Hilbert transform of the time series $x_i(t)$ (in our case an EEG signal), and PV denotes the Cauchy principal value. The instantaneous phase is then

$$\varphi_i(t) = \arctan \frac{\tilde{x}_i(t)}{x_i(t)} \quad (5)$$

Beforehand, for each subject and each single-trial, a filter bank using a series of band-pass FIR (Finite Impulse Response of length 450 ms) filters was used to extract, from the EEG signal, seven frequency bands corresponding to the low (Lα: [8-10] Hz; Lβ: [13-20] Hz; Lθ: [4-5] Hz) and the high (Hα: [11-13]; Hβ: [21-35]; Hθ: [6-7] Hz) components of the alpha (α), beta (β), and theta (θ) bands. The gamma frequency (γ; [36-44] Hz) was also extracted. For each band and each time-window, both the classical spectral coherence and the PLV were computed for electrodes F3, F4, T7, C3, C4, T8, P3, P4, O1 and O2 with respect to Fz for each trial (it must be noted that this montage could also be used with an EEG cap having a reduced number of sensors). For the same reasons as those previously mentioned, the computed phase synchronization values were also standardized using equation (1). The only difference is that P_i represents the electrophysiological parameter, i.e., here a given EEG phase synchronization value between two given electrodes, and SP_i represents its standardized value. The SP_i values were then averaged across blocks and subjects.

F. Curve Fitting

For each sensor and each block, the average phase synchronization changes (across subjects) were fitted with a linear model from which the coefficient of determination (R^2) and its slope were obtained. The pair of electrodes that showed a fit indicating a coefficient of determination

capable of explaining at least 50% of the variability of the data (i.e., $R^2 \geq 0.50$) was selected, and the slopes of these linear models were statistically tested. To further evaluate any correlation between kinematics and EEG data, MT and ML versus phase synchronization were plotted for each selected pair. An examination of the data led us to consider a linear and a logarithmic model to fit these relationships. The best fit was selected by considering the coefficient of determination, the Root mean square error of the Fit (RmseF), and the sum of squares due to the fitting error.

III. Results

The results revealed a linear decrease of the PLV during movement planning and execution for the electrode pair Fz-F3, Fz-F4, Fz-T7, Fz-C3, Fz-P3, Fz-P4, and Fz-O1. These changes were also correlated with improved kinematics throughout adaptation. Since classical coherence and PLV gave similar results and considering the advantages of the PLV, we will only present the results related to the latter.

A. Kinematics Results

As expected, the sudden introduction of the rotational perturbation caused distorted movement trajectories and slow progression towards the targets during the early exposure phase whereas as the subject adapted, these trajectories became straighter and smoother revealing that the subjects were learning the internal model of the novel visuomotor perturbation (i.e., the new tool) [3]. Such behavioral improvement was reflected by the significant decrease (Wilcoxon test, $p<0.0013$) of MT and ML from the early to the late exposure period (Fig. 1A,B).

B. Electrophysiological Results

More interestingly, while kinematics improved during adaptation; electrophysiological changes in phase synchronization were simultaneously observed (Fig. 1C). Namely, as the subjects adapt, the electrodes pair Fz-F3 (Lα), Fz-F3 (Lβ), Fz-F4 (Lβ), Fz-C3 (Lβ) and Fz-O1 (γ) revealed a decrease captured by a linear model (i.e. $R^2 \geq 0.50$) for both movement planning and execution (Fig. 2). For planning, the slopes of these linear models were significantly different from zero (*t-test*, $p<0.05$) for Fz-F3 (Lα;Lβ), Fz-C3 (Lβ), Fz-O1 (γ) and during execution for Fz-F3 (Lα) and Fz-C3 (Lβ) while a trend was observed for Fz-F3 (Lβ, p=0.06) and Fz-F4 (Lβ, p=0.07). Also, for execution, the same analysis revealed that the electrode pairs Fz-F3 (Hθ), Fz-T7 (Lθ), Fz-P3 (Hα) and Fz-P4 (Hα) showed a significant linear decrease of the PVL (*t-test*, $p<0.05$) throughout adaptation.

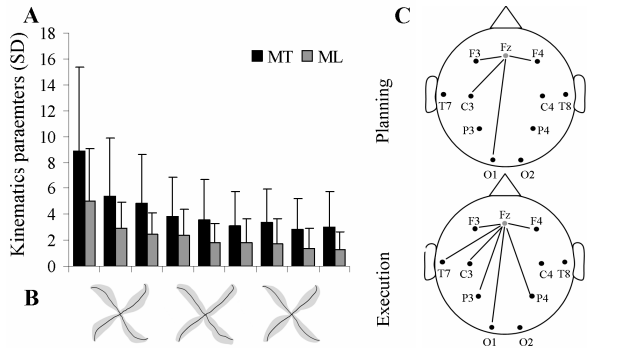

Fig.1. Changes in kinematics and PLV throughout adaptation. (A) Changes in MT and ML. (B) Changes in path throughout learning. (C) Pair of electrodes showing a decrease in synchronization throughout adaptation during planning (top scalp plot) and execution (bottom scalp plot).

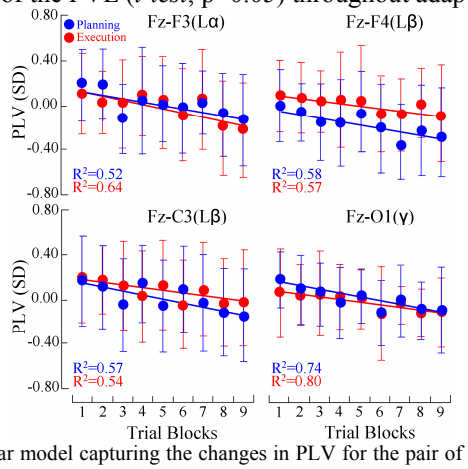

Fig.2. Linear model capturing the changes in PLV for the pair of electrodes Fz-F3 (Lα; upper left panel), Fz-F4 (Lβ; upper right panel), Fz-C3 (Lβ; bottom left panel) and Fz-O1 (γ; bottom right panel).

C. Correlation and Fitting Analysis

The results for the correlation analyses showed that the relationships between the changes in PLV for the pairs Fz-F3, Fz-F4, Fz-C3, Fz-O1 and the MT and ML values were best fitted by using a logarithmic curve ($R^2 \geq 0.40$, $RmseF<0.52$).

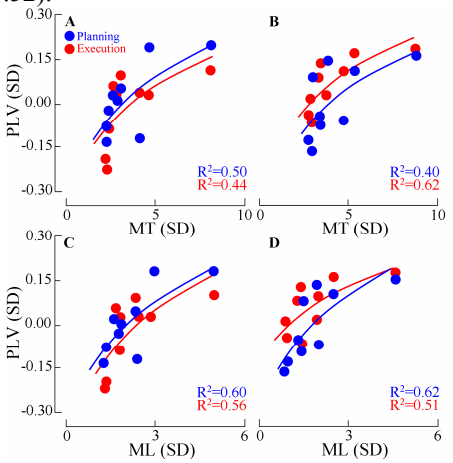

Fig.3. Representation of the PLV versus MT (first row) and ML (second row) for both movement planning (blue) and execution (red). (A, C) Pair Fz-F3 (low alpha band). (B,D) Pair Fz-C3 (low beta band).

IV. Discussion

The main findings of this study are that the subjects showed a linear decrease in phase synchronization as they adapted to a new tool for the pair of electrodes Fz-F3, Fz-F4, Fz-T7, Fz-C3, Fz-P3, Fz-P4, and Fz-O1 during movement planning and execution. These results reinforce the idea that decreased phase synchronization reflects a refinement of cortical resources by attenuating non-essential communication, inducing an improvement in kinematics [4].

Therefore, these linear changes in phase synchronization that mirror human motor performance throughout adaptation

may provide potentially relevant brain biomarkers for tracking human learning/adaptation status when the learning of a new tool takes place. Specifically they could play a significant role in a broad range of applications related to brain monitoring and cognitive-motor status assessment. It must be noted that the biomarkers provided here do not contradict, but instead complement, those previously proposed [3]. Indeed, there is a need to combine several measurements using both univariate (e.g., spectral power) and multivariate (e.g., spectral coherence, PLV) techniques to obtain non-invasive, robust brain biomarkers.

One potentially interesting role of such biomarkers would be to overcome some well-known difficulties related to BCI systems such as the need to use adaptive decoding, constant recalibration and the maintenance of stable performance while a user tries to control a neuroprosthesis [8]. A BCI system is a tool that the user learns to control by changing his/her cortical dynamics in an appropriate way (if sufficient feedback is provided). Such an adaptation relies mainly on the capacity of the user's brain to change its cortical dynamics since generally the decoding parameters are fixed. Therefore, if the user's performance degrades, frequent recalibrations of the decoding algorithms are required [8].

In order to address these problems [9], some studies have proposed adaptive algorithms [10]. However, these approaches use supervised adaptation based on *a priori* knowledge of an external target. This actually represents a major pitfall for practical BCI applications since the user needs to decide when and where to direct his/her intentions. In ecological situations no external target is available [11]. Thus, these unresolved issues [12] may be solved by using the biomarkers evidenced here since they offer a new possibility to overcome this type of difficulty by providing reinforcement signals to guide the decoding process. The EEG biomarkers presented here might help to solve such important drawbacks by constantly adapting the decoding algorithm to the subject's mental states, allowing thus, a stable co-adaptation/cooperation between the user and the BCI system. For example, the PLV computed for the low beta frequency band between the pairs of electrodes Fz-F3 and Fz-C3 could be computed using a sliding window (e.g., 15-20 trials). Then, if the PLV at these sites increases, indicating a poor performance by the user, the decoding algorithm parameters should be updated to compensate by using, for instance, a reinforcement learning signal. Alternatively, if the user adapts as indicated by a reduction of the PLV for the same sites and bands, no parameter adjustments are needed.

The use of such biomarkers could also reveal the sources of alterations in behavioral performance, which cannot be revealed by kinematic parameters alone. For instance, poor learning/adaptation performance could be due to other factors such as stress or fatigue. These factors relate to an increased phase synchronization and generally for different electrodes pairs and/or frequency bands than those used here [13-14]. Therefore, these brain biomarkers can track the level of performance but also decipher or indicate potential causes of poor learning performance. As previously mentioned, these PLV (multivariate) brain biomarkers complement well those derived from univariate methods such as spectral power. It is important to realize that changes in phase synchronization for a specific frequency range do not necessarily imply similar power changes for the same electrodes [15]. For future real-time EEG ecological applications, brain biomarkers for individual subjects and single trials need to be available. Since EEG signals are highly variable from one trial to another, the combination of several brain biomarkers such as phase synchronization and spectral power will offer cross-information. Such information could provide robust, accurate, non-invasive brain biomarkers of motor performance and also insight into possible reasons for the failure of sensorimotor adaptation.

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