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# Signal processing for non-invasive brain biomarkers of sensorimotor performance and brain monitoring

Rodolphe J. Gentili, Hyuk Oh, Trent J. Bradberry,
Bradley D. Hatfield and José L. Contreras-Vidal
*University of Maryland-College Park*
*USA*

## 1. Introduction

Many endogenous and exogenous factors can affect the physiological, mental and behavioral states in humans. In order to identify such states, monitoring tools need to use biological indicators, or biomarkers, able to identify biological events and predict outcomes. These biomarkers can be divided into two categories.

The first category contains what we could call the "structural" biomarkers that are extracted from physiological structures and mainly defined at the genetic and/or molecular level (e.g., Berg, 2008; Dengler et al., 2007; Eleuteri et al., 2009; Isaac, 2008; Moura et al., 2008; Wei, 2009). For instance, the formation or consumption of certain molecules provide biomarkers to identify patients with moderate to severe forms of cardiac heart failure (Eleuteri et al., 2009; Isaac, 2008) while changes in cortisol level allow detection of an increased stress response (Armstrong & Hatfield, 2006). Similarly, other active molecules (e.g., C-reactive protein) are used as biomarkers of valvular heart disease (Moura et al., 2008) while cardiac troponins and N-type natriuretic peptides can be used in post-transplant patient surveillance (Dengler et al., 2007). Other examples of structural biomarkers aim to identify abnormalities in neural connectivity in the brain. For instance, the presence of certain molecules in venous blood or a damaged white matter provides potential predictors of risk of cerebral palsy (Dammann & Leviton, 2004, 2006; Kaukola et al., 2004). Also, genomic and proteomic biomarkers are able to define the risk of an individual to develop a neurodegenerative disease such as Parkinson's disease (Gasser, 2009), Alzheimer's disease (Berg, 2008; Wei, 2009) or amyotrophic lateral (Tuner et al., 2009) and multiple sclerosis (Wei, 2009).

The second category includes what we could call "functional" biomarkers that are further related to continuous measurements of body function throughout time in order to track physiological, mental and behavioral states (e.g., Georgopoulos et al., 2007; Hejjel & Gál, 2001; Hofstra et al., 2008). For instance, electro-cardiograms, heartbeat, and body temperature are possible functional biomarkers to determine stress level (Hejjel & Gál, 2001). Body temperature can be used to detect the phase of circadian rhythms (Hofstra et al.,

2008), and blood pressure can be employed to identify the chronic fatigue (Newton et al., 2009). Recently, it has been also suggested that measurements of the skin conductance was a better tool to monitor nociceptive stimulation and pain than heart rate and blood pressure (Storm et al., 2008).

Another important family of functional biomarkers includes status measurements of brain functions in order to monitor and interpret neural activity, identify specific neurological events and predict outcomes (e.g., Gentili et al., 2008; Guarracino, 2008; Hatfield et al., 2004; Irani et al., 2007; Tuner et al., 2009; van Putten et al., 2005; Williams & Ramamoorthy, 2007). These brain indicators, or brain biomarkers, can be derived from signals recorded by means of invasive acquisition techniques such as implantable microelectrodes arrays or electrocorticography (Schalk et al., 2008), or, alternatively, non-invasive techniques such as electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI) or emerging neuroimaging technologies such as functional near infrared spectroscopy (fNIRS) (Irani et al., 2007; Parasuraman & Rizzo, 2007). For instance, brain biomarkers derived from temporal or spectral EEG signals processing allow for the determination of anesthetic depth during pediatric cardiac surgery (Williams & Ramamoorthy, 2009). Other brain biomarkers derived from EEG, such as the brain symmetry index, permit the detection of seizure activity in the temporal lobe and can be, therefore, useful for epileptic monitoring needed in intensive care units (van Putten et al., 2005). Still using EEG analysis, it is also possible to detect a reduction of cerebral blood flow below a certain threshold (Guarracino et al., 2008). Other high-temporal resolution measurement techniques such as MEG have also been used to successfully classify respective groups of individuals subjected to multiple sclerosis, Alzheimer's disease, schizophrenia, Sjögren's syndrome, chronic alcoholism, facial pain and healthy controls (Georgopoulos et al., 2007). More recently, it has been shown that the fNIRS imaging technique, a relatively novel cerebral imaging tool, could provide information allowing the monitoring of brain oxygenation by measuring regional cerebral venous oxygen saturation (Guarracino et al., 2008).

These examples provided by medical, biomedical and bioengineering research fields illustrate how various brain monitoring tools are being developed intending to uncover structural or functional brain biomarkers for detection, prevention, prediction, and diagnosis of heart function, adverse neurological events and neural/neurodegenerative diseases. However, the research aiming to uncover functional brain biomarkers directly relevant for the restoration of cognitive-motor and/or sensorimotor functions (e.g., disabled populations, advanced aging) is still a relatively young research field. Indeed, although many assistive technologies aiming to restore cognitive-motor and sensorimotor functions are currently underway (e.g., neuroprosthetics (Cipriani et al., 2008; Wolpaw et al., 2007); exoskeletons (Carignan et al., 2008)), few brain monitoring tools related to sensorimotor integration are being developed. However, these bioengineering applications, such as the design of smart neuroprosthetics, require a deeper understanding of brain dynamics in ecological situations that involve human interaction with new tools and/or changing environments that guide learning and more generally shape motor behavior. Specifically, such monitoring tools aiming to assess the dynamic status of the brain necessitates the knowledge of brain biomarkers able to track brain dynamics in ecological situations where humans have to learn new tasks, to master novel tools and/or changing environments. These brain biomarkers should be preferably non-invasive (i.e., no surgical intervention

needed), simple to record and analyze, simultaneously robust and sensitive to specific changes in brain function in natural situations. Such assessment in ecological situations requires non-invasive recording of the dynamic brain activity with a high temporal resolution (e.g., millisecond), which is well suited for EEG. Although some research efforts are underway (e.g., Deeny et al., 2003, 2009; Gentili et al., 2008, 2009a,b; Hatfield et al., 2004; Haufler et al., 2000; Kerick et al., 2004) to develop methods to provide non-invasive functional brain biomarkers able to track the brain status during sensorimotor performance; some questions and problems remain. For example, how accurately and efficiently can a cognitive-motor or sensorimotor state be inferred? What methods might provide robust brain biomarkers applicable on single-subject and single-trial bases? How can the signal processing techniques used in laboratory contexts to derive such biomarkers can be transferred successfully in real-time applications to ecological contexts? Although this manuscript does not purport to exhaustively answer these questions, some elements of response and possible problem-solving perspectives will be presented and discussed.
Therefore, the aims of this chapter are to provide the state-of-the-art of the research along with the main signal processing techniques related to functional non-invasive EEG/MEG brain biomarkers that allow tracking of cortical dynamics to assess the level of mastery of a sensorimotor task and the adaptation to novel tools or environments. It must be noted that, from a technical point of view, the methodological approaches presented here are also applicable to some (minimally) invasive techniques such as electrocorticography. However, when considering an invasive approach, in addition to the inherent risks and difficulties related to a surgical intervention, the whole scalp will not be likely covered by the recording device, creating limitations in terms of the regions of interest where potential biomarkers could be detected. Thus, we will mainly focus on non-invasive recording techniques that use a high-temporal resolution (EEG/MEG) with a particular emphasis on results obtained with EEG since this recording technique is portable and, thus, applicable in ecological situations. In Section 2, the main pre-processing methods employed to clean the EEG/MEG signals of artifacts will be explained along with the subsequent methodological approaches that allow for the computation of brain biomarkers. Specifically, Section 2 will focus on the spectral power and phase synchronization representing the two most classical univariate and multivariate non-invasive functional brain biomarkers of performance. In Section 3, the classical and the latest findings in this brain biomarker research field will be presented by emphasizing promising progress but also current limitations and possible solutions to overcome them. Section 4, will present how these brain biomarkers may provide important advances in bioengineering applications in ecological contexts such as the development of smart neuroprosthetics and brain monitoring techniques. Finally, we will summarize these results and suggest future research directions.

## 2. Signal Processing Methods

The aim of this second section is not to provide an exhaustive presentation of all the existing processing methods for EEG and MEG signals, but rather, to introduce some signal processing approaches for EEG and MEG signals to, first, pre-process the signal to remove artifacts and, then, to derive non-invasive functional brain biomarkers (e.g., based on spectral power and coherence) that are used to assess and track adaptation in cognitive-motor/sensorimotor performance in humans.

### 2.1 Pre-processing

During recording, EEG/MEG signals are generally corrupted with some undesirable artifacts such as body movements, muscular artifacts, eye movements, eye blinks, environmental noise or heart beat. These artifacts produce possible biases in the detection and interpretation of brain biomarkers that will be later derived from the EEG/MEG signals. Constraints placed on subjects to minimize these artifacts in a laboratory setting cannot be realistically expected in an ecological situation. Therefore, in order to remove such artifacts, pre-processing of the EEG/MEG signals may be a necessary and critical step (Georgopoulos et al., 2007). Although several signal processing methods are available, such pre-processing stage can be performed by using various methods such as Independent Component Analysis (ICA) and adaptive filtering.

#### 2.1.1 Artifact removal using Independent Component Analysis

In many dynamical systems, the measurements are given as a set of mixed signals with noise. For example, in the same way conversations are recorded by a number of microphones in a crowded party, brain signals containing artifacts are measured through multiple EEG/MEG sensors. The information in each of the original signals can be analyzed as long as it is possible to identify the system corresponding to the source that emits these signals captured by a set of sensors. In this regard, blind source separation is a relevant method to approximately recover the original source signals from a set of observed mixed signals without any *a priori* knowledge about either the source signals or the mixing system. Regarding applications in biomedical signal processing, ICA is currently considered one of the most sophisticated statistical approaches for solving the general problem of blind source separation.

##### 2.1.1.1 Basic assumptions of ICA

ICA is a linear transformation method to find estimated source signals (i.e., the independent components) while optimally demixing the mixed signals where independent components must satisfy the following conditions (Hyvärinen & Oja, 2000; Oja, 2004; Vaseghi, 2007; Vigário et al., 2000):

i) The independent components are non-Gaussian and statistically independent of the higher-order statistics (covariance and kurtosis).
ii) At most, no more than one independent component can be Gaussian.
iii) The dimension of the set of independent components does not exceed the number of sensors.

Moreover, three additional assumptions must be considered when ICA is applied to EEG/MEG signals (Hyvärinen et al., 2001):

iv) The existence of statistically independent components in EEG/MEG source signals is assumed.
v) The statistically independent components are instantaneously and linearly mixed at the sensors.
vi) The independent components and the mixing processes are supposed to be stationary.

Several versions of ICA exist. First, the simple ICA will be presented. Then, the two most popular ICA algorithms named Infomax ICA and FastICA will be reviewed.

#### 2.1.1.2 Simple ICA algorithm

In the simple ICA algorithm, the unknown additive noise is excluded (Oja, 2004). Assume that the $m$ dimensional observed signal (e.g., EEG/MEG) vector $\mathbf{x}(k) = [x_1(k), \quad x_2(k), \quad \cdots, \quad x_m(k)]^T$ is given by a linear combination of the $n$ dimensional source signal vector $\mathbf{s}(k) = [s_1(k), \quad s_2(k), \quad \cdots, \quad s_n(k)]^T$ at each time sample $k$, that is:

$$x_i(k) = a_{i1}s_1(k) + a_{i2}s_2(k) + \cdots + a_{in}s_n(k), i = 1, 2, \cdots, m. \tag{1}$$

In a more compact notation, Equation (1) can be rewritten as

$$\mathbf{x}(k) = \sum_{j=1}^{n} \mathbf{a}_j s_j(k) = \mathbf{A}\mathbf{s}(k) \tag{2}$$

where the matrix $\mathbf{A} = [\mathbf{a}_1, \quad \mathbf{a}_2, \quad \cdots, \quad \mathbf{a}_n]$ is the mixing matrix, the indices n and m are the number of sensors and sources, respectively. The matrix A is a m x n matrix (generally m ≥ n but a common choice is m = n). Practically, both the mixing matrix and the source signal vector are unknown; however, we can estimate a demixing matrix $\mathbf{W}$ in order to obtain the estimation of a source signal vector $\hat{\mathbf{s}}(k)$ using three fundamental assumptions (from i) to iii); see section 2.1.1.1) for ICA previously mentioned such that:

$$\hat{\mathbf{s}}(k) = \mathbf{W}\mathbf{x}(k) \tag{3}$$

where ideally $\mathbf{W} = \mathbf{A}^{-1}$ and the elements of $\hat{\mathbf{s}}(k)$ are statistically independent.
Practically, several preprocessing strategies make ICA simpler and better conditioned (Hyvärinen & Oja, 2000). For example, the centering technique simplifies the ICA algorithms by subtracting the mean vector from the observed signal vector so as to make it a zero mean valued vector. On the other hand, whitening decreases the correlation among the observed signals by transforming the centered observed vector to have unit variance in all directions (Vigário, 2000).

#### 2.1.1.3 Infomax ICA and FastICA

Among the various ICA algorithms that are available, Infomax ICA (Bell & Sejnowski, 1995) and FastICA (Hyvärinen, 1999) are the two most popular ones. They use different independence properties to obtain the independent components. Specifically, Infomax ICA

minimizes the mutual information whereas FastICA maximizes the non-Gaussian nature. These two algorithms provide qualitatively and quantitatively similar results. However, FastICA is generally faster than Infomax ICA, but is subject to more variability than Infomax ICA especially when applied to removal of eye blink artifacts (Glass et al., 2004). Concerning Infomax ICA, this approach is unable to separate source signals with a sub-Gaussian distribution. Therefore, an extended version of Infomax ICA, named extended Infomax ICA, has been introduced to separate both sub-Gaussian and super-Gaussian distributions for the source signals (Lee et al., 1999).

#### 2.1.1.4 Independent Components Analysis for artifact identification and removal from EEG and MEG signals

ICA has been recently applied to the analysis of biomedical signals mostly acquired from EEG and MEG. In these applications, it is essential to associate each independent component with the neurophysiological nature of the phenomenon (e.g., event-related brain dynamics, steady-state brain activity, etc.) in order to identify them. In many cases, ICA algorithms have been successfully applied to EEG and MEG in order to identify and remove artifacts such as cardiac, ocular, or muscular activities from the neurophysiological activities of interest (the computational steps of these algorithms are illustrated in Fig.1), since the nature of the artifact sources is different from those of the actual brain activity related sources in terms of anatomical, physiological, and statistical considerations.

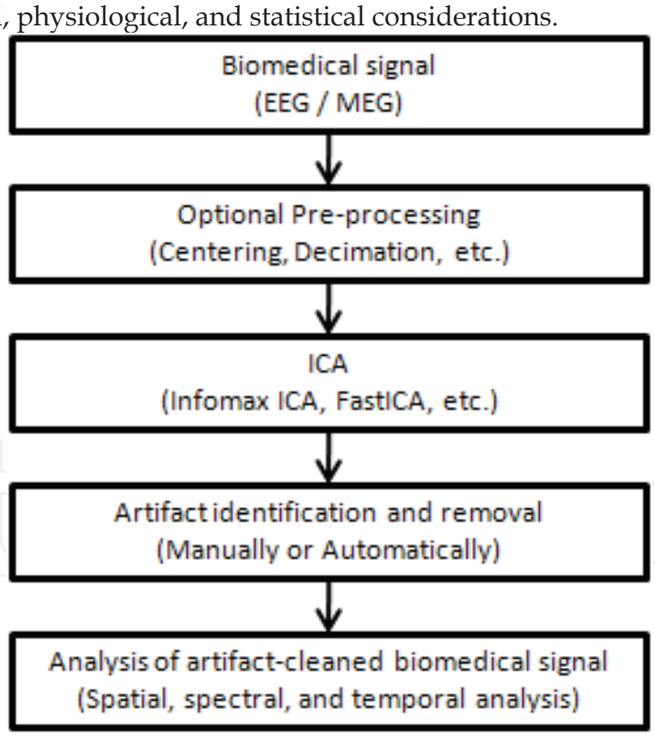


Fig. 1. Computational steps for ICA-based signal processing.

In general, the independent components related to the suspected artifacts must be manually assigned to an artifact type based on the attributes of the independent components (e.g., amplitude peak, frequency patterns). However, since the criteria to decide to remove such a component can depend of subjective judgments, this approach is sensitive to biases.

Recently, several automatic artifact detection and removal methods have been introduced (Delorme et al., 2001; Rong & Contreras-Vidal, 2006). For example, the functionally similar independent components could be automatically categorized using neural network with respect to a set of features such as spatial maps, spectral properties, and higher-order statistics (Rong & Contreras-Vidal, 2006).

#### 2.1.1.5 Limitation of ICA

Although ICA facilitates the analysis of the brain dynamics, this method cannot isolate highly correlated sources due to the assumption of statistical independence. Furthermore, it cannot identify uniquely ordered, correctly phased and properly scaled source signals, in other words, when using ICA, the independent components that are isolated could be randomly ordered, reversely phased, or ill scaled. However, in the case where such specific characteristics are of interest, it must be noted that ICA is not able to identify the source of the signals. Moreover, for practical bioengineering applications, artifact identification and removal based on ICA is not appropriate for real-time processing since it requires significant computational resources and a large amount of data collected from a sufficiently large number of channels. The next paragraph introduces adaptive filtering, another method that can be potentially useful for real-time applications.

### 2.1.2 Artifact removal using adaptive filtering

Despite the advantages of ICA as an artifact removal method, this technique is computationally very expensive and, thus, not well suited under some conditions such as real-time applications. However, other linear and nonlinear filtering based-techniques to remove specific artifacts in real-time are available. Among these methods, adaptive filtering has been introduced for removing ocular artifacts in real-time (He et al., 2004).

#### 2.1.2.1 Principle of adaptive filtering

Adaptive filters are based on the principle that the desired (clean) signal can be extracted from the input signal through the adaptation of the filter parameters. The filter parameters are adapted based on minimizing an error function between the filter output signal and a desired signal. The most commonly used adaptive filtering algorithms are the Kalman filter, the least mean square (LMS) filter, and the recursive least square (RLS) filter (for more details on the implementations of these methods see Zaknich, 2005).

#### 2.1.2.2 Removing ocular artifacts by adaptive filtering

Specifically, adaptive filtering has been used to remove ocular artifacts that could contaminate EEG/MEG (Georgiadis et al., 2005; Sanei & Chambers, 2007). For instance, He et al., (2004) suggested an adaptive filter that uses three inputs to the system. First, the actual EEG/MEG signal $x(k)$ with the ocular artifacts $z(k)$ as the primary input ($s(k) = x(k) + z(k)$). The second and third inputs are the vertical and horizontal eye movement (VEOG and HEOG) as two reference inputs ($r_v(k)$ and $r_h(k)$), respectively. Each reference input is first processed by a finite impulse response (FIR) filter using the RLS algorithm ($\hat{r}_v(k)$ and $\hat{r}_h(k)$, respectively) and then subtracted from the EEG signal under

the assumption that the desired ocular artifacts cleaned EEG signal is a zero-mean stationary random signal that is uncorrelated with the ocular artifacts and the two reference signals. Thus, the desired output produced by the whole system is the EEG signal without ocular artifacts. Hence the whole system can be described using the following sets of equations and the corresponding scheme illustrated in Fig. 2:

$$e(k) = s(k) - \hat{r}_v(k) - \hat{r}_h(k) = x(k) + \left[z(k) - \hat{r}_v(k) - \hat{r}_h(k)\right] \tag{4}$$

where $\hat{r}_v(k) = \sum_{m=1}^{M} h_v(m) r_v(k+1-m)$ and $\hat{r}_h(k) = \sum_{m=1}^{M} h_h(m) r_h(k+1-m)$ for the filter parameters $h_v(m)$ and $h_h(m)$, respectively. $e(k)$ is the error between the observed signal and reference inputs.

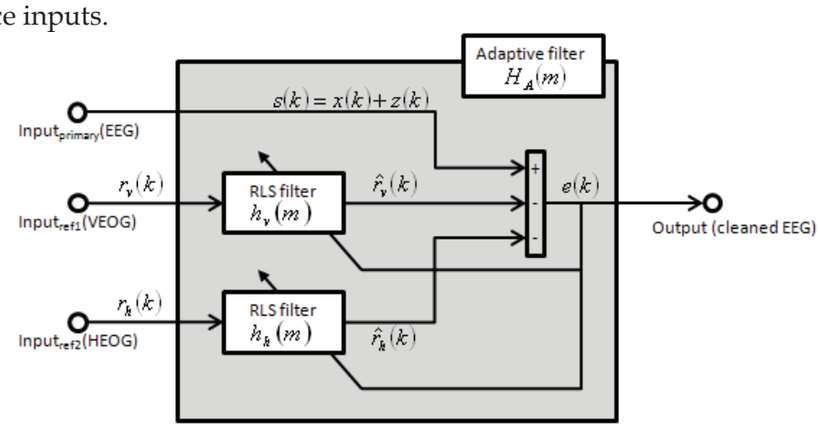


Fig. 2. Computational scheme of the adaptive filter configuration for eye artifact removal (EOG: Electrooculography). (The different symbols used in this figure are described in the text above).

#### 2.1.2.3 Limitation of adaptive filtering

The LMS and RLS filters, popular alternative algorithms to the Kalman filter, also present some advantages and drawbacks. The LMS filter is one of the relatively simple adaptive filtering algorithms, so it is computationally very efficient, but it is not suitable for signals with high rate of sudden changes due to its slow rate of convergence (Vaseghi, 2007). In this case, the RLS filter offers relatively faster convergence and smaller error rate with more computations. More generally, a single type of artifact can be removed with a single filter, so multiple filtering must be performed when multiple forms of artifacts are present, increasing the chances of distorting the signals of interest.

### 2.1.3 Summary

To summarize, many novel artifact-removal techniques have been introduced along with some of their variants (He et al., 2004; Lee et al., 1999; Vaseghi 2007; Vigário et al., 2000). A common requirement for the artifact removal method is to remove the artifacts but keep the neurophysiological activities of interest intact. For this reason, the employment of algorithms for modeling and filtering must be carefully considered along with their

underlying assumptions, since it may undesirably alter the estimated artifact-cleaned EEG/MEG signal (Hyvärinen & Oja, 2000; Oja, 2004; Vaseghi, 2007; Vigário et al., 2000). ICA is generally the most suitable artifacts removal algorithm with minimal affects on the interesting EEG/MEG signals, but it is very expensive in terms of both computation and memory usage. Adaptive filtering, on the other hand, can effectively remove artifacts from EEG/MEG signals in real-time fashion.

Once EEG/MEG signals are free of artifacts, the next step is to compute the brain biomarkers derived from these clean EEG/MEG signals in order to assess sensorimotor performance and learning. In this regard, the two main biomarkers that are available are derived from the spectral power and phase synchronisation between two signals located at different positions on the scalp. These two brain biomarkers are presented in the next two sections.

### 2.2 Spectral Power

A first type of brain biomarker that can be used to assess the level of mastery in sensorimotor performance and learning can be derived from the spectral power computed for specific frequency bands. Many different methods (e.g., parametric, non-parametric, and subspace methods) are available to compute the EEG/MEG spectral power (Kay, 1988; Sanei & Chambers, 2007; Shumway & Stoffer, 2000). For instance, some of these methods that have been applied are the classical fast Fourier transform (e.g., Hatfield et al., 1984; Haufler et al., 2000) and more sophisticated procedures such as the multitaper (e.g., Conteras-Vidal & Kerick, 2004) or wavelet (e.g., Mu et al., 2008) techniques. While some of these approaches have been applied with success in EEG/MEG studies that focus on sensorimotor performance and/or Brain Computer Interface (BCI) systems (McFarland et al., 2006; Pfurtscheller & Lopes da Silva, 1999), two methods are particularly popular to compute the EEG/MEG spectral power. The first approach uses autoregressive (AR) methods (e.g., McFarland et al., 2006, 2008) while the second one uses the band power method (Pfurtscheller & Lopes da Silva, 1999, 2005; Pfurtscheller & Neuper, 2006) providing changes in power amplitude that are often referred to as "event related desynchronization (ERD)" and "event related synchronization (ERS)."

#### 2.2.1 Autoregressive filtering

The first technique that consists of using AR models is a classical parametric method (Marple, 1987; Sanei & Chambers, 2007; Shumway & Stoffer, 2000). Contrary to the fast Fourier transform, parametric spectral estimation by means of AR models offers various advantages by presenting a more general and flexible framework for parsimonious dynamical modeling of time series data useful for different applications such as prediction, classification or causality analysis of time series (Shumway & Stoffer, 2000; Wong et al., 2006). Specifically, an AR filter can be used for linear prediction in order to model the signal of interest; here an EEG or MEG signal. Namely, the real EEG/MEG signal can be considered as the sum of the signal modeled by the AR filter and an error term. Thus, by subtracting the real EEG/MEG signal to the one filtered by the AR model, the prediction error can be determined (Fig.3).

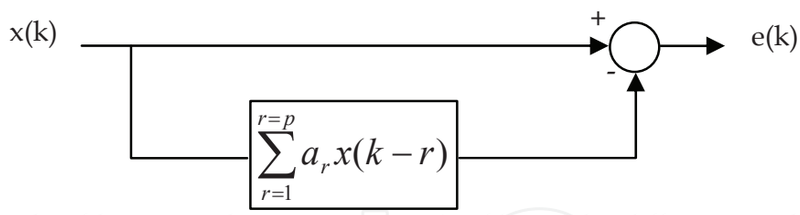


Fig. 3. Principle of linear prediction using an AR filter. (The different symbols used in this figure are described in the text below).

The prediction error for an AR model is defined as:

$$e(k) = x(k) - \sum_{r=1}^{r=p} a_r x(k-r) \tag{5}$$

where $a_r$ ($r$ = 1,2,3,…,p) are the coefficients, the constant $p$ is the order of the filter, and $k$ denotes the discrete time sample. $x(k)$ and $e(k)$ are respectively the input signal to approximate and the prediction error. For a given $p$, the coefficients are identified by minimization (e.g., LMS, Durbin method) of the error or driving signal that is considered to be zero mean white noise.

By applying the z-transform to equation (5) and considering Z= $e^{j\omega}$ we obtain:

$$\frac{X(\omega)}{E(\omega)} = \frac{1}{1 - \sum_{r=1}^{r=p} a_r e^{-jr\omega}} \tag{6}$$

Where $E(\omega)$ represents the power spectrum of the white noise that is constant (i.e., $E(\omega) = K_\omega$), and $X(\omega)$ represents the power spectrum of the signal. From this model, the spectral power can be estimated for any specific frequency band.

AR models may suffer from poor estimation of the model parameters mainly due to the limited length of the measured signal (Sanei & Chambers, 2007) while the order of the AR filter may influence the precision of the computation of power spectrum. For instance, McFarland et al., (2008) recently showed that the resolution of lower frequency signals requires higher AR model orders and also that increasing AR model order provided an enhanced spectral resolution. It must be noted that an increase of the AR model order results in a higher computational cost even if the tremendous advances in digital signal processor and field-programmable gate-array technology tend to weaken this drawback (Wang et al., 2006). Also, in the case of non-stationarity, parametric spectral estimation may also be applied with a moving window (Ozaki & Tong, 1975) or using some alternative approaches avoiding, thus, the introduction of such a moving window (Wong et al., 2006).

### 2.2.2 ERD/ERS method

The second method is well-established and has been successfully applied to many different EEG/MEG investigations (Gentili et al., 2008 ,2009a, 2009a; Kerick et al., 2004; Pfurtscheller & Lopes da Silva, 1999, 2005; Pfurtcheller & Neuper 2006; Tombini et al., 2009). Specifically, this method computes the spectral power by squaring and averaging across trials the output of a band pass filter in order to detect the changes in power amplitude. ERD and ERS correspond respectively to a decrease and an increase of the spectral power for specific frequency bands (e.g., alpha band) and brain regions (e.g., frontal region). These measures are often expressed as a percentage of a decrease or increase with respect to a baseline condition preceding task performance and are computed according to the following equation (for more details see Pfurtscheller & Lopes da Silva, 1999):

$$ERS/ERD = \frac{P_E - P_R}{P_R} \times 100\ (\%) \tag{7}$$

where $P_E$ and $P_R$ correspond to the power computed within the frequency band of interest in the period after the event begins and during the preceding baseline or reference period, respectively.

It must be noted that although these ERD/ERS quantifications can be computed using different methods including AR filters, (e.g., see Table 1 in Pfurtscheller & Lopes da Silva, 1999) the term ERD/ERS is generally associated with the band pass method (see Pfurtscheller & Lopes da Silva, 1999, 2005 for a comprehensive review). From a physiological point of view, ERD/ERS mirror variations of the activity of local interactions between main neurons and interneurons that control the frequency components of the ongoing EEG (Pfurtscheller & Lopes da Silva 1999, 2005). As previously mentioned, although several methods can be used to isolate some specific frequency bands; one of the main problems of the EEG/MEG spectral analysis is the definition of the upper and lower bounds of the bands (Pfurtscheller & Lopes da Silva, 1999). Although the definition of the frequency band limits can slightly differ from one study to another, a possible approach for partitioning the frequency bands related to human motor performance for healthy adults is to consider the theta ([4-7 Hz]), alpha ([8-13 Hz]), beta ([14-35 Hz]) and gamma ([36-44 Hz]) frequency bands (e.g., Hatfield et al., 2004; Haufler et al., 2000; Tombini et al., 2009). Sometimes, the frequency range spread from 8 to 15 Hz (Blankertz & Vidaurre, 2009) or from 9 to 13Hz (Blankertz et al., 2009; Pfurtscheller & Neuper, 1997) are also named alpha frequency (or mu rhythm under certain conditions). Moreover, since it has been shown that certain frequency sub-bands are related to specific brain states during a sensorimotor task (e.g., Contreras-Vidal et al., 2004; Gentili et al., 2008; Hatfield et al., 2004; Tombini et al., 2009), most of the EEG/MEG studies refined their analysis by considering sub-frequency bands, typically, the low and high component of the original entire band. Therefore, for the bands previously defined, the low theta ([4-5 Hz]), high theta ([6-7 Hz]), low alpha ([8-10 Hz]), high alpha ([11-13 Hz]), low beta ([14-23 Hz]) and high beta ([24-35 Hz]) frequency bands can also be considered. In addition to the classical gamma band ([36-44 Hz]) it is also possible to consider the extended gamma band spread from 45 to 100 Hz or higher. This gamma band extension can be divided into several sub-bands with a method using a 10-Hz-wide band with an overlap of 5 Hz frequency bins ranging from 45 to 100 Hz (Crone et al.,

1998). Although, as previously mentioned, the limits of these bands can slightly change from one study to another; many EEG/MEG investigations consider frequency bands where upper and lower limits of the bandpass filter is the same for all the subjects tested. It must be noted that another approach (Pfurtscheller & Lopes da Silva, 1999, 2005) defines these frequency band limits for each individual subject in order to take into account some inter-individual differences. For instance, three possible methods can be used to determine the upper and lower limits of the bandpass filter; i) detection of the most reactive frequency band by comparing the two short-term power spectra; ii) use of a continuous wavelet transform; iii) definition of frequency bands relative to the spectral peak frequency (for more details see Pfurtscheller & Lopes da Silva, 1999, 2005).

### 2.3 Phase synchronization: Coherence and Phase Locking Value

Another important brain biomarker of sensorimotor performance can also be provided by analyzing the phase synchronization between different cortical sites. Such phase synchronization measures the level of interaction and cross talk among EEG/MEG channels allowing the identification of how signals propagate within the neural network of the brain. These spatial EEG/MEG coherence measures, generally presented for individual frequency bands, result from correlations among different cortical sources. Therefore, spectral coherence is a common method for determining synchrony in EEG/MEG activity.

Regarding the literature aiming to find brain biomarkers for human sensorimotor performance and learning, spectral power analysis has been widely used for a long time, however, the use of spectral coherence is relatively more recent, while the phase locking value (PLV), despite its advantages, still remains rarely used in this field. Generally, the literature focusing on EEG/MEG signal analysis computes the synchronization between two time signals recorded from two electrodes $x$ and $y$ by using classical coherence (Nunez & Srinivasan, 2006). First the cross-spectrum (CS) has to be computed using the following equation:

$$CS_{xy}(f) = \left\langle S_x(f)\overline{S}_y(f) \right\rangle \tag{8}$$

where $S_x(f)$ is the Fourier transform of the signal $s_x(t)$, $\overline{S}_x(f)$ is the complex conjugate of the Fourier transform of the signal $s_x(t)$ and $\langle\ \rangle$ is the expectation operator. Then, the complex coherence (CC) is computed by using the cross-spectrum normalized with respect to the two corresponding spectra of the two signals. Thus we have:

$$CC_{xy}(f) = \frac{CS_{xy}(f)}{\sqrt{CS_{xx}(f)CS_{yy}(f)}} \tag{9}$$

Where $CS_{xy}(f)$ is the cross-spectrum of the two time signals $s_x(t)$ and $s_y(t)$ and $CC_{xy}(f)$ the complex coherence.

Finally, the coherence (C) can be calculated by considering the absolute value of the complex coherence:

$$C_{xy}(f) = \left| CC_{xy}(f) \right| \tag{10}$$

Another way to interpret these equations is to consider the following equation:

$$S_x(f) = \rho_x e^{j\varphi_x} \tag{11}$$

where the Fourier transform $S_x(f)$ of the signal $s_x(t)$ is expressed in order to explicitly illustrate its amplitude $\rho_x$ and its phase $\varphi_x$ (here $j$ denotes the imaginary unit and $j^2$=-1) .

Now the cross-spectrum expressed in equation (8) can be rewritten as:

$$CS_{xy}(f) = \left\langle \rho_x \rho_y e^{j\Delta\varphi} \right\rangle \tag{12}$$

where $\Delta\varphi$ denotes the phase difference between the two signals (i.e., $\Delta\varphi = \varphi_x - \varphi_y$).
Thus, the complex coherence expressed in equation (9) can be rewritten as:

$$CC_{xy}(f) = \frac{\left\langle \rho_x \rho_y e^{j\Delta\varphi} \right\rangle}{\sqrt{\left\langle \rho_x^2 \right\rangle \left\langle \rho_y^2 \right\rangle}} \tag{13}$$

Leading to the classical coherence provided by the following equation:

$$C_{xy}(f) = \left| \frac{\left\langle \rho_x \rho_y e^{j\Delta\varphi} \right\rangle}{\sqrt{\left\langle \rho_x^2 \right\rangle \left\langle \rho_y^2 \right\rangle}} \right| \tag{14}$$

Although this measure of classical coherence is usually used in EEG/MEG studies, two main drawbacks have to be considered (Lachaux et al., 1999). First, the coherence can be applied only to stationary signals. Most of the time this assumption of stationarity (in time or across trials) is not strictly valid, however, the measure of phase-locking does not require this assumption on the signal. Second, coherence does not specifically quantify phase relationships. In fact, coherence increases with amplitude covariance (see the presence of the signal amplitudes $\rho_x$ and $\rho_y$ in the numerator and denominator of the formula in equation (14)) implying an uncertainty concerning the relative importance of amplitude and phase covariance in the coherence. In other words, the coherence does not separate the effects of amplitude and phase in the interrelations between two signals. Thus, based on these

premises and since phase-locking provides a measure that is sufficient to conclude if two brain regions interact, another measure of phase synchronization, the PLV, has been introduced, offering, thus, an alternative measure only based on the detection of phase covariance (Lachaux et al., 1999; Le Van Quyen et al., 2001; Tass et al., 1998).
Before computing the PLV, the frequency bands and sub-bands of interest mentioned in Section 2.2.2 are extracted for each subject and each single-trial by means of a filter bank using band-pass FIR (Lachaux et al., 1999) or IIR filters (Brunner et al., 2006).

Then, the PLV can be computed for each frequency band. Contrary to the classical coherence, it is defined by only considering the phases of the two signals.

$$PLV = \left| \left\langle e^{j\Delta\varphi} \right\rangle \right| \tag{15}$$

where $\Delta\varphi$ denotes the phase difference between the two signals $s_x(t)$ and $s_y(t)$ (i.e., $\Delta\varphi = \varphi_x - \varphi_y$).

It must be noted that equations (14) and (15) are comparable; however, the equation expressing the PLV does not include the amplitudes of the two signals, allowing examination of synchronization phenomena in EEG/MEG signals by directly capturing the phase synchronization.
Two methods to compute the phases $\varphi_x$ and $\varphi_y$ are available. The first one (Lachaux et al., 1999) uses a complex Gabor wavelet as defined by equation (16):

$$G(t,f) = e^{-a} e^{j2\pi ft} \tag{16}$$

Where a= $-\frac{t^2}{2\sigma_t^2}$, $t$ represents the time and $\sigma$ is the standard deviation of the Gaussian envelope.
The second method (Tass et al., 1998) uses the Hilbert transform as defined by the following equation:

$$\widetilde{s}_x(t) = \frac{1}{\pi} PV \int_{-\infty}^{+\infty} \frac{s_x(t)}{t-\tau} d\tau \tag{17}$$

In this definition, $\widetilde{s}_x(t)$ is the Hilbert transform of the time series $s_x(t)$ (in our case an EEG/MEG signal), and PV indicates that the integral is taken in the sense of Cauchy principal value. The instantaneous phase can then be calculated as:

$$\varphi_x(t) = \arctan \frac{\widetilde{s}_x(t)}{s_x(t)} \tag{18}$$

It must be noted that these two methods provide very similar results when applied to EEG data (Le Van Quyen et al., 2001).
The averaging process can be performed either over time (i.e., in equation (19), n ∈ [1…N], where *n* is the sample number of the time series) for single-trial applications such as BCI approaches (Brunner et al., 2006; Lachaux et al., 2000) or over trials (Lachaux et al., 1999) (i.e., in equation (19), n ∈ [1…N], where *n* is the trial number). Thus, equation (19) is obtained:

$$PLV = \frac{1}{N}\left|\sum_{i=1}^{N} e^{j\Delta\varphi(t,n)}\right| \tag{19}$$

where $\Delta\varphi(t,n)$ is the phase difference and $\Delta\varphi(t,n) = \varphi_x(t,n) - \varphi_y(t,n)$.

As for the coherence, the PLV is ranged from 0 to 1 indicating that during this time window the two channels considered are ranged from unsynchronized to perfectly synchronized, respectively. It must be noted that, despite the previously mentioned advantages of the PLV, it has been also suggested that one reason to use coherence rather than the PLV directly is that coherence measures are weighted in favor of epochs with large amplitudes. In particular, more consistent phase estimates will be probably obtained when amplitudes are large (if large amplitudes show a large signal-to-noise ratio as is generally the case in EEG/MEG) (Nunez & Srinivasan, 2006). Therefore, both coherence and PLV measures can be used. Interestingly, due to their unique advantages and pitfalls, some studies apply and compare both techniques that, in the case of convergence, lead to robust results, although in the case of EEG both approaches are subject to the electrode reference problem that can distort such measurements (Nunez & Srinivasan, 2006). Recently, Darvas et al., (2009) have proposed an extension of the PLV, called bi-PLV that is specifically sensitive to non-linear interactions providing, thus, robustness behavior to spurious synchronization arising from linear crosstalk. This property is particularly useful when analyzing data recorded by EEG or MEG. From a physiological point of view, both coherence and PLV methods quantify the magnitude of correlation, for a given frequency (or band), between different areas of the cerebral cortex. Thus, high coherence and/or PLV implies substantial communication between different cortical areas while low coherence and/or PLV reflects regional autonomy or independence (Nunez & Srinivasan, 2006).

## 3 Non-Invasive Functional Brain Biomarkers of Human Sensorimotor Performance:

Although the signal processing approaches described above are applicable to both EEG and MEG signals, we will focus mainly on brain biomarkers derived from EEG since, as mentioned in the introduction, this technique is portable and therefore is particularly well suited for ecological motor tasks such as aiming (e.g., marksmanship, archery), drawing, arm reaching and grasping task. Therefore, most of the examples below will present the results of brain biomarkers derived from EEG signals.

### 3.1 Spectral power

A series of studies that began in the early 80's provided a growing body of evidence that it is possible to assess the cortical dynamics of motor skills in novice and expert performers during visuomotor challenge such as marksmanship and archery tasks. These studies revealed changes in EEG activity with skill learning as well as differences in EEG power between novice and expert sport performers (Del Percio et al., 2008; Hatfield et al., 1984, 2004; Haufler et al., 2000; Kerick et al., 2004; Landers et al., 1994; Slobounov et al., 2007). Specifically, the power computed for the alpha and theta frequency bands were positively related to the level of motor performance (Del Percio et al., 2008; Hatfield et al., 2004; Haufler et al., 2000; Kerick et al., 2004).

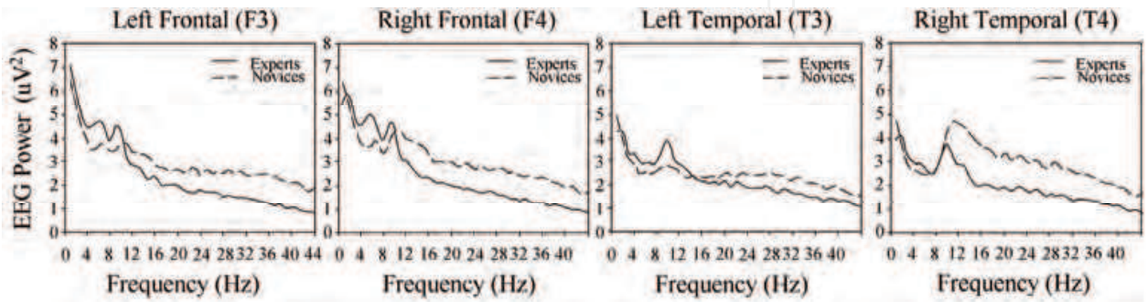


Fig. 4. Mean EEG power (mV²) spectra (1–44 Hz) at left and right homologous sites in the frontal and temporal regions during the aiming period of the shooting task for expert marksmen versus novice shooters (Adapted from Haufler et al., (2000) with permission from Elsevier Science).

For instance, Haufler et al., (2000) showed that, compared to novices, experts revealed an overall increase in EEG alpha power in the left temporal lobe (i.e., T3) while the same comparison between novices and experts performing cognitive tasks that were equally familiar to them did not provide any differences. The authors concluded, therefore, that the EEG alpha power differences observed were likely due to the difference of level in mastery of the motor task (see Fig. 4). Obviously, the differences in cortical dynamic between novices and experts revealed by these studies were accompanied with important differences between performances (i.e., the novices scored lower and exhibited more variability in their performance than the experts). Thus, these studies provided brain biomarkers (e.g., alpha power) able to identify a high level of motor performance resulting from an extensive practice period, without, however, considering the changes of such brain biomarker throughout the training period itself.

Interestingly, in a more recent study Kerick et al., (2004) extended these investigations by assessing the dynamic changes throughout a marksmanship intensive training for novices during three months. The results revealed that, throughout the training, the performance for the shooting task was enhanced (Fig. 5A) concomitantly with an increased EEG alpha power (Fig. 5B) at the temporal level located on the contralateral side (i.e., T3, left temporal lobe) while such observation was not observed when the subjects were at rest. Such EEG changes are generally interpreted as indicative of high levels of skill and associated with a cortical refinement leading to reductions of nonessential cortical resources (Hatfield & Hillman, 2001). This kind of neural adaptation process may result in simplification of neurocognitive activity and less possibility of interference with essential visuomotor processes. Within an

activation context, a decrease in alpha power frequency band (i.e., desynchronization) represents an activated cortical site. Conversely, an increase in alpha power (i.e., synchronization) corresponds to a reduction of activation of a given cortical region (Pfurtscheller et al., 1996) indicating a decrease of the recruitment of neural resources.
In addition to the alpha frequency band, several studies suggested that theta oscillations are also related to performance enhancement (Caplan et al., 2003; Tombini et al., 2009). For instance, during a virtual maze navigation task, Caplan et al., (2003) observed that theta oscillations reflected an updating of motor plans in response to incoming sensory information that facilitates the information encoding of participant's cognitive map.

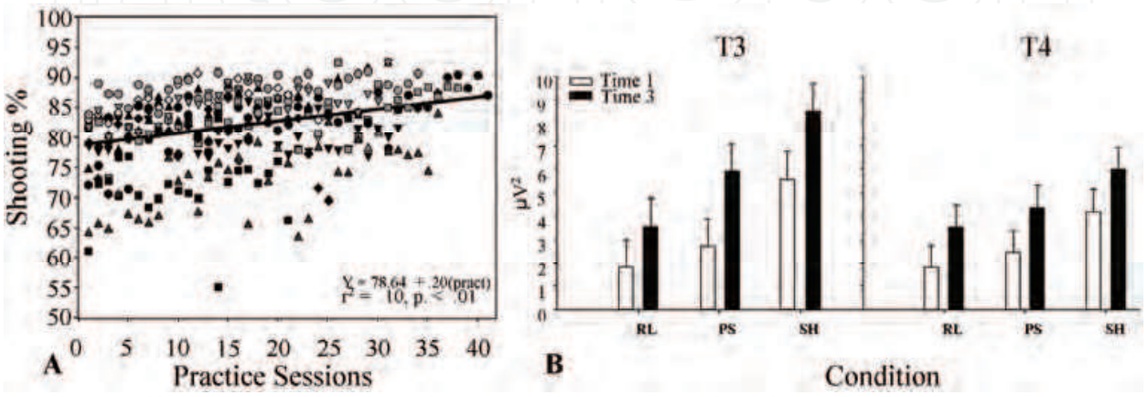


Fig. 5. A. Shooting percentages by practice session. The slope of the linear regression revealed a significant increase in performance over all practice sessions from time 1 to 3 (equation lower right corner). The different symbols represent the performance scores of individual participants on separate days of practice. B. Changes in mean power from time 1 to 3 during shooting (SH), postural (PS), and Baseline (BL) condition (T3, left panel; T4, right panel). (Adapted from Kerick et al., (2004) with permission from Wolters Kluwer/Lippincott Williams).

Although other interpretations of theta power increases are plausible (e.g., frontal theta EEG synchronization could also reflect an increased short term memory load; for a review see Klimesch et al., 2008), a growing body of work suggest that theta oscillations are functionally associated with error monitoring (Cavanagh et al., 2009; Larson & Lynch, 1989; Smith et al., 1999; Yordanova et al., 2004).
Thus, taken together these studies suggested that changes in alpha and theta power can be used as non-invasive functional brain biomarkers capable either to assess the level of mastery of a given sensori-motor task (e.g., marksmanship task) and/or to track the brain status during motor practice. However, these studies used visuomotor task where upper limb movements were extremely specific (e.g., archery, marksmanship task) without considering more familiar movements used in daily activities such as arm reaching, grasping and tool or object manipulations. Moreover, these investigations addressed the improvement of an established motor ability (e.g., Haulfer et al., 2000), or a long learning period of a skill involving no interference with previous motor experience (e.g., Caplan et al., 2003; Kerick et al., 2004). Interestingly, Kranczioch et al., (2008) showed that the learning of a visuomotor power grip tool led to EEG changes in spectral power and cortico-cortical coupling (i.e., coherence). However, this study did not involve a tool that required

suppression of a familiar response. Nevertheless, in daily activities, we frequently need to adapt our motor commands related to our upper limb to learn new input-output mappings characterizing novel tools by inhibiting familiar behavior or responses that are no longer valid to manipulate them. Such tool learning requires the selection and guidance of movements based on visual and proprioceptive inputs while frontal executive function would inhibit the pre-potent input-output relationships during acquisition of the internal model (also called internal representation) of the new tool. This would be typically the case if a person has to learn to manipulate a new tool such as a neuroprosthetic. It should be noted that Anguera et al., (2009) used a visuomotor adaptation task requiring suppression of preexisting motor responses in order to quantify the changes in error-related negativity associated with the magnitude of the error. However, this study did not focus on tracking the learning process by using brain biomarkers derived from spectral power and/or phase synchronization.

Based on this rational, a recent study (Gentili et al., 2008) intended to address this problem by analyzing the cortical dynamics during the learning of a new tool having unknown kinematics features. In this experiment, fifteen right-handed healthy adults subjects sat at a table facing a computer screen and, with their right hand, had to perform "centre-out" drawing movements (on a digitizing tablet) linking a central target and one of four peripheral targets. Movement paths were displayed on the screen, but a horizontal board prevented any vision of the moving limb on the tablet. EEG signals were acquired using an electro-cap with 64 tin electrodes, which was fitted to the participant's head in accordance with the standards of the extended International 10-20 system (Fig.6). 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) ten subjects (i.e., learning croup) had to adapt to a $60^{o}$ counter clock-wise screen cursor rotation. In addition, five healthy (i.e., control group) subjects were examined using the same protocol but in the absence of any visual distortion. Movements were self-initiated and targets were self-selected one at a time. All the targets were displayed throughout each trial. The instructions were to draw a line as straight and as fast as possible linking the home target and the peripheral target. 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 providing, thus, an extended time-window to analyze cortical activations related to preparation processes (i.e., planning) of the movement.

In order to quantify the motor performance during both movement planning and movement execution periods, the Movement Time (MT), Movement Length (ML) and Root Mean Square of the Error (RMSE) were computed from the 2D horizontal displacements. The MT was defined as the elapsed time between leaving the home circle and entering the target. The ML was defined as the distance traveled in each trial.

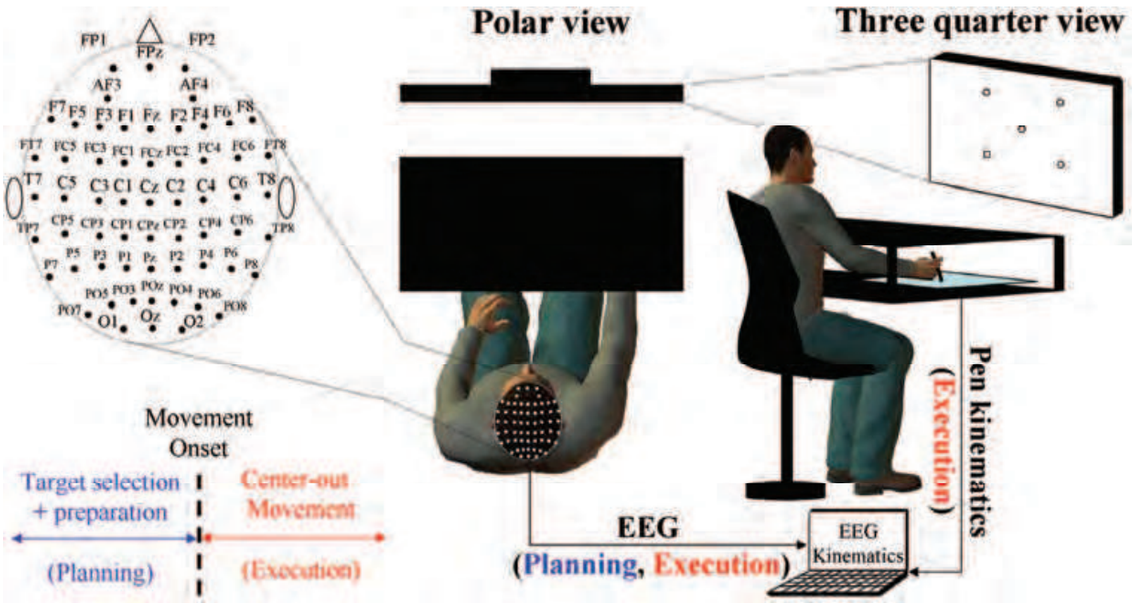


Fig. 6. Experimental device to record kinematics and EEG signals during the visuomotor adaptation task. Subjects sat at a table facing a computer screen located in front of them at a distance of ~60 cm and had to execute the motor task which consisted of drawing a line on a digitizing tablet (represented in light blue on the figure) that was displayed in real-time on the computer screen. The home target circle was the origin of a direct polar frame of reference, and the target circles were positioned 10 cm from the origin disposed at 45°, 135°, 225°, and 315°. Once a successful trial was performed, to prevent any feedback, all visual stimuli were erased from the screen in preparation for the next trial.

The RMSE was computed to assess the average deviation between the movement trajectory from the 'ideal' straight line connecting the home and the pointing target. 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 subject's performance during the pre-exposure phase (i.e., baseline condition) and to focus on changes due solely to adaptation, the MT, ML and RMSE values were standardized with respect to the pre-exposure stage.
Continuous EEG data were epoched in 2-s windows centered at movement onset. Both pre- (i.e., planning) and post- (i.e., execution) movement time-windows 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. The EEG signals were cleaned by means of the ICA Infomax method applied on a single-trial basis described in section 2.1.1. For each subject and each single-trial, the EEG power (ERS/ERD) were computed by squaring and integrating the output of a dual band-pass Butterworth fourth order filter, and standardized with respect to the pre-exposure stage. The EEG power was computed for the alpha (low: 8-10 Hz, high: 11-13 Hz), beta (low: 13-20 Hz, high: 21-35 Hz); theta (Low: 4-5 Hz, High: 6-7 Hz) and γ (36-44 Hz) bands. The entire alpha, beta and theta frequency bands were also analyzed. For the alpha band, two similar frequency ranges have been considered. i) alpha1: spread form 8 to 13Hz, and ii) alpha2: spreads from 9 to 13 Hz. For each sensor and each block, the average power changes (across subjects) were fitted using a linear model from which the coefficient of determination ($R^2$) and its slope were

obtained. The sensors that showed a fit indicating a coefficient of determination capable to explain at least 50% of the variability of the data (i.e., $R^2 \geq 0.50$) allowed us to determine the sensor clusters and the frequency bands of interest. The results of this procedure led us to consider the two alpha frequency bands and the high component of the theta frequency band for the right (FT8, T8, TP8) and left (FT7, T7, TP7) temporal and right (FP2, AF4, F4, F6, F8) and left (FP1, AF3, F3, F5, F7,) frontal lobes. This procedure led us also to consider the two alpha frequency bands for the left (P1, P3, P5, P7, PO3, PO5, PO7) and right (P2, P4, P6, P8, PO4, PO6, PO8) parietal and left (O1) and right (O2) occipital regions (For the electrodes sites see Fig. 6). It must be noted that the results for both alpha bands were similar. However, since the findings for the second alpha band (i.e., [9-13Hz]) were slightly better only this frequency band will be presented and discussed. For the alpha (i.e., [9-13Hz]) and high theta (i.e., [6-7Hz]) bands and the eight clusters of interest, the average power values were computed, and the same fitting process was applied. Furthermore, in order to investigate any correlation between the kinematics data and the EEG power, the average EEG power values obtained for the clusters of interest were plotted versus the MT, ML and RMSE values. Exponential (single and double), linear and quadratic models were used to fit these relationships. The best fit was selected by considering the coefficient of determination and its adjusted value, the mean square error of the fit, and the sum of squares due to the fitting error.

The results showed that, during the early learning phase, the subjects performed distorted movement trajectories with a slow progression towards the targets. However, as the subjects of the learning group learned the unknown physical (kinematics) properties of the novel tool, the analysis of the motor performance revealed that the MT, ML and RMSE decreased throughout adaptation (Fig. 7A-C). From the early to the late learning period, the trajectories were straighter and smoother while the control group did not show any performance improvement (Fig. 7A-C).

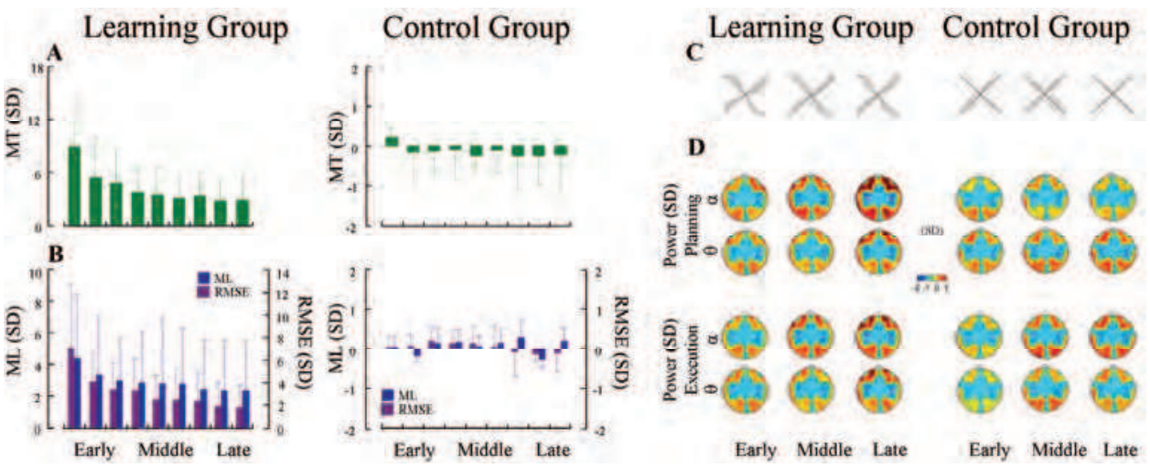


Fig. 7. Concomitant EEG and kinematic changes throughout learning for the learning and control groups. (A) Changes in MT (±SE) throughout the learning blocks. (B) Changes in ML (±SE) (purple) and RMSE (±SE) (blue) throughout the learning blocks. (C) Changes in average trajectory (thick black lines) throughout learning for early, middle and late exposure (the grey area represents the standard error across subjects). (D) Qualitative EEG changes in alpha (first and third row) and high theta (second and fourth row) frequency bands for the

frontal, temporal, parietal and occipital regions during planning (two first rows) and execution (two last rows). For the sake of clarity, sensors which did not belong to the clusters of interest were set to the minimal value of the scale for the scalp plot. The results of the learning group and control group are represented in the left and right column, respectively. (Adapted from Gentili et al., (2008) with permission from EURASIP).

Simultaneously to these behavioral changes, the results revealed that, as the subject adapt, the alpha and the high component of the theta power increased in the frontal and temporal lobes whereas an increased in alpha power also took place in the parietal lobes. Moreover, these spectral changes occurred during both movement planning (i.e., movement preparation) and movement execution. It must be noted that this alpha frequency band spread form 9 to 13Hz showed the largest reactivity during the adaptation to the novel tool and thus provides a better brain biomarker. Contrary to the learning group, the control group did not exhibit any changes in spectral power (Fig. 7D).

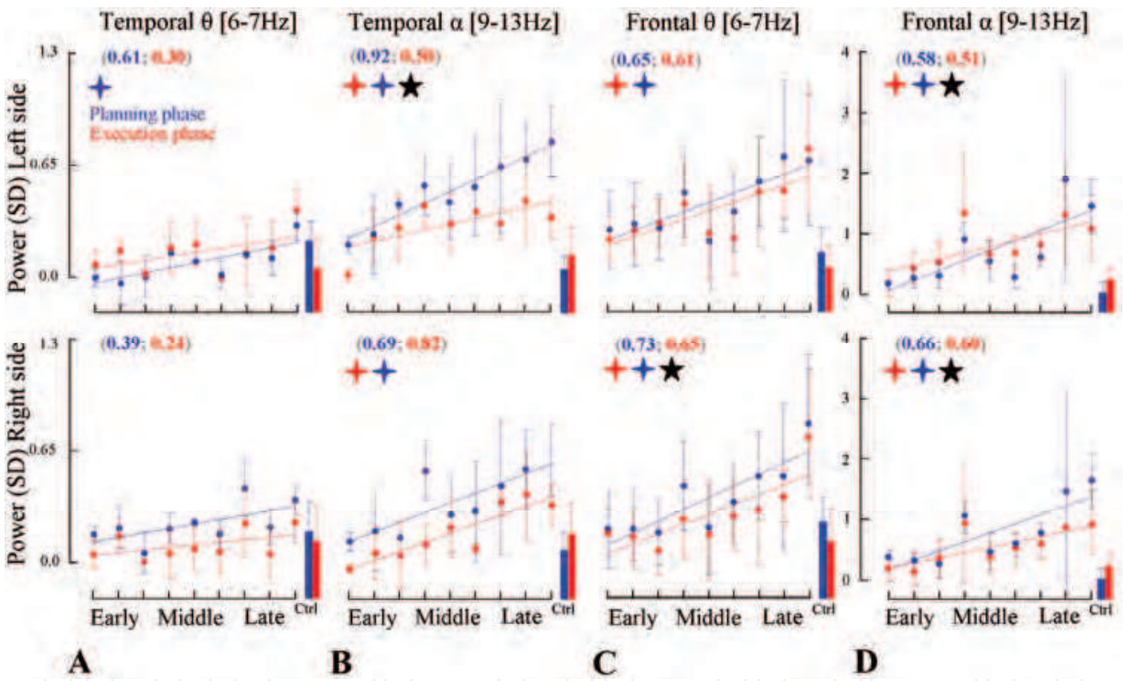


Fig. 8. Linear fits of EEG power changes for the frontal and temporal clusters for the participants of the learning group. Standardized values of the average EEG power computed across subjects (n=10) of the learning group and blocks (n=9) for the alpha and the high theta frequency bands recorded from the right (FT8, T8, TP8) and left (FT7, T7, TP7) temporal lobes and right (FP2, AF4, F4, F6, F8) and left (FP1, AF3, F3, F5, F7) frontal lobes. The blue and red stars indicate that the slopes were significantly different from zero for planning and execution, respectively. The black star indicates that the slopes between planning and execution were significantly different. The two bars on the right side of each panel represent the average value of the EEG power for the same cortical sites and the same frequency band for planning (blue) and execution (red) of the control group. (Adapted from Gentili et al., (2008) with permission from EURASIP).

Among the various models tested to fit these spectral changes, the best model that was able to capture these changes was linear. Only the left temporal lobe presented a significantly linear increase for the high component of theta power during movement planning (Fig. 8A). However, for the frontal lobes, the same linear theta power increase occurred during both movement planning and execution with similar slopes (Fig. 8C). For both the temporal and frontal lobes, the alpha power significantly increased linearly during both movement planning and execution. The slopes were also different between movement planning and execution (Fig. 8B, D). Finally, the alpha power showed a significant linear increase in the left and right parietal lobes for the planning while only a tendency was observed for the execution and both movement stages for the two occipital lobes (Fig. 9A, C).

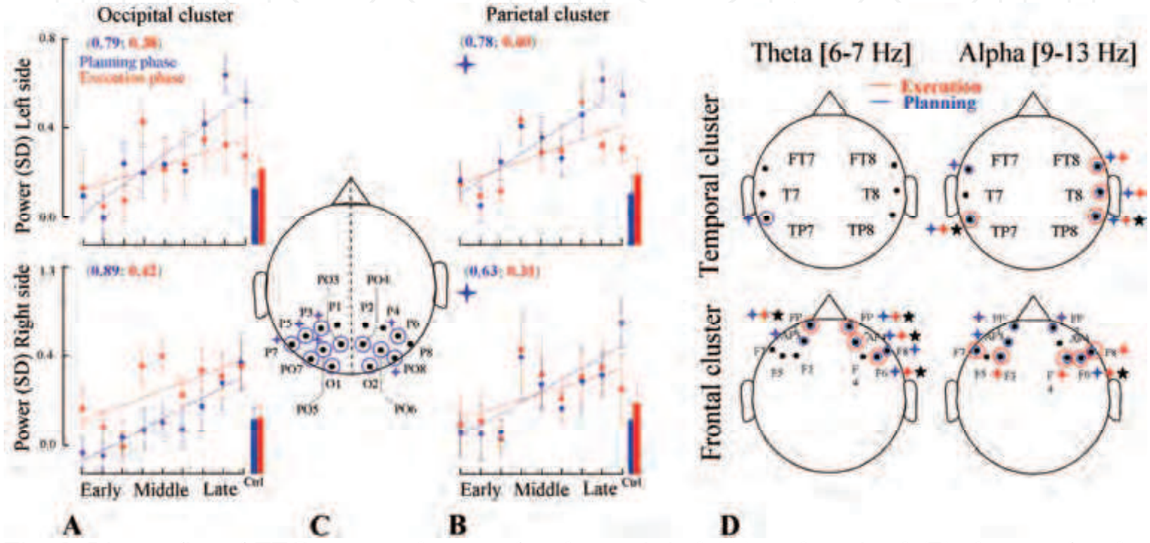


Fig. 9. Linear fits of EEG power changes for the occipital (A) and parietal (B) clusters for the learning group. Standardized values of the average EEG power computed across subjects (n=10) and blocks (n=9) for the alpha frequency bands recorded from the right (O2) and left (O1) occipital lobes and right (P2, P4, P6, P8, PO4, PO6, PO8) and left (P1, P3, P5, P7, PO3, PO5, PO7) parietal lobes. The blue stars indicate that the slopes were significantly different from zero for planning. The two bars on the right side of each panel represent the average value of the EEG power for the same cortical sites and the same frequency band for planning (blue) and execution (red) for the control group. The scalp plot depicts the clusters of electrodes in the occipital and parietal sites (C) and also for the frontal and temporal sites (D). For both panels, the blue and red circles indicate that the linear models for the alpha and theta power showed a coefficient of determination ($R^2$) greater than 0.5 for the planning and execution of movement, respectively. The blue and red stars indicate that the linear models had a slope significantly different from zero for planning and execution phases, respectively. The black star indicates that the slopes for planning and execution are significantly different from each other.

The previous results were obtained at a cluster level; however, a refined analysis conducted at the sensor level also showed that these linear changes where located on specific sensors (Fig. 9C, D) for these two frequency bands and both movement planning and execution. Finally, in order to find a correlation model between these spectral changes and those observed in kinematics during performance several models have been tested.

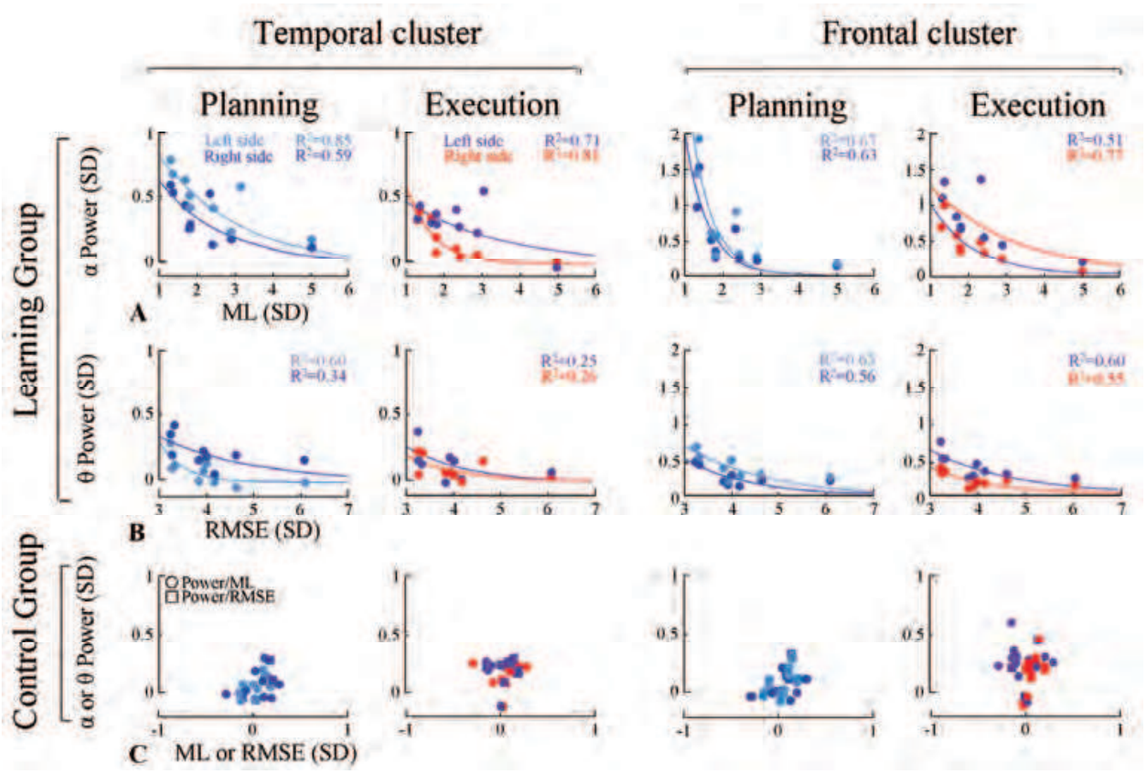


Fig. 10. Changes in EEG power in the alpha and high theta bands versus kinematics. The first two rows represent the average values of the standardized power of the alpha bands computed for the right and left temporal and frontal regions during planning and execution versus the concomitant changes in ML (first row) and RMSE (second row) for the learning group. The third row represents the same relationship for both alpha versus ML and high theta versus RMSE for the control group. (Adapted from Gentili et al., (2008) with permission from EURASIP).

The findings showed that, among the models tested, the single exponential was able to capture with the best accuracy these co-variations between EEG power changes and the corresponding motor production (Fig. 10A, B). The control group did not show any changes (Fig. 10C).

Thus, it appears that these changes in theta and alpha power provide informative brain biomarkers to track the cortical dynamics in order to assess the level of performance and also to track during both planning and execution the level of mastery of a novel tool throughout learning. Although useful, this first type of brain biomarker has the drawback to be univariate, that is, the power computed at a particular scalp site is able to characterize activation patterns for a particular channel (or brain region) without accounting for functional network connectivity or communications between different regions of the cortex during performance. It must be noted that these spectral power changes have been robustly observed in EEG/MEG studies and represent today a classical brain biomarker of human performance. Beside the spectral power, another type of brain biomarker, derived from EEG/MEG, is the computation of the phase synchronization between two scalp sites. Although initially less popular, this second technique (see section 2.3) is increasingly used to

track the level of sensorimotor performance/learning. Recently this approach led to interesting results that will be presented in the next section.

### 3.2 Phase synchronisation

Contrary to the previously mentioned investigations focusing on the spectral power analysis, there are only a few studies that analyzed the cortical networking by means of coherence and/or PLV to assess the level of motor performance and/or to track the learning dynamic. For instance, Bell and Fox (1996) reported a decreased EEG coherence in experienced infant crawlers relative to novice crawlers and attributed their findings to a pruning of synaptic connections as crawling became more routine. Another experiment, further directly related to our purpose and conducted by Deeny et al., (2003), compared EEG coherence between a frontal site (i.e., sensor Fz) and several other cortical regions in two groups of highly skilled marksmen who were similar in expertise, but who differed in competitive performance history. One of the two groups performed consistently better in competition and exhibited significantly lower coherence between the left temporal region (i.e., T3) and the premotor area (i.e., Fz) in the low-alpha (8–10 Hz) and low-beta (13–22 Hz) bandwidths during the aiming period (Fig. 11).

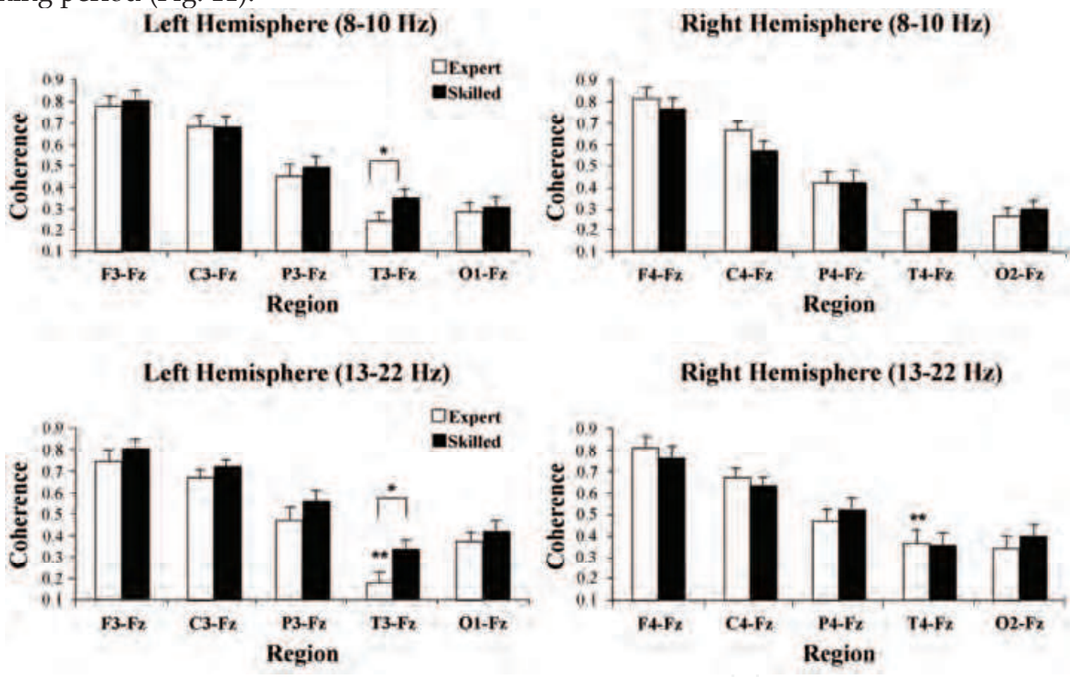


Fig. 11. Upper row. Expert and skilled group means for low-alpha (8–10 Hz) coherence estimates between Fz (premotor area) and frontal, central, temporal, parietal, and occipital sites in each cerebral hemisphere. Lower row. Expert and skilled group means for low-beta (13–22 Hz) coherence estimates between Fz (premotor area) and frontal, central, temporal, parietal, and occipital sites in each cerebral hemisphere. *Significant difference, $p < 0.05$; **T3–Fz coherence was significantly lower than T4–Fz coherence in the expert group only. (Adapted from Deeny et al., (2003) with permission from Human Kinetics Publishers).

More recently, Deeny et al., (2009) confirmed that the coherence could also be useful to assess the brain dynamic in relation to the level of mastery of a motor task. Specifically, they

showed that experts generally exhibited lower coherence over the whole scalp compared with novices, with the effect most prominent in the right hemisphere. Coherence was positively related to aiming movement variability in experts (Fig. 12).

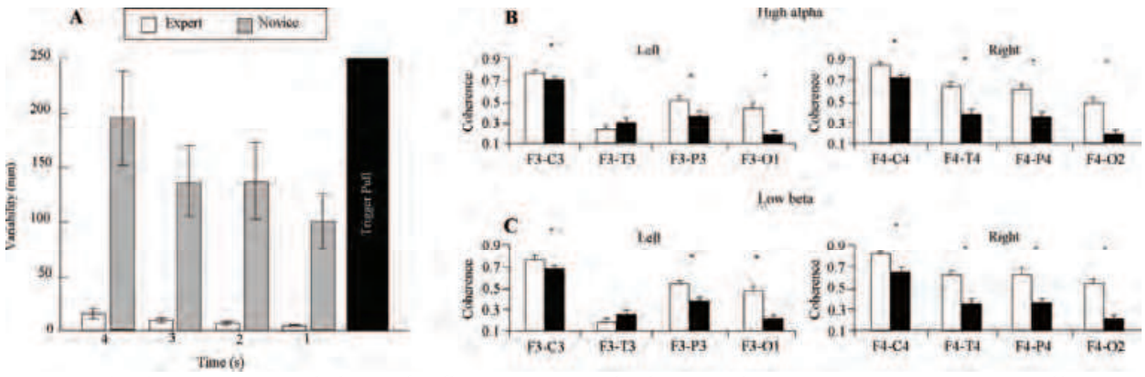


Fig. 12. A. Average variability of rifle aiming path during the 4 s prior to trigger pull in 1-s time bins for experts and novices. Error bars represent standard error. B. Coherence values for high alpha. C. Coherence values for low beta. *Indicate significantly higher coherence in novice shooters relative to experts ($p$ <0.05). C = central; F = frontal; O = occipital; P = parietal; T = temporal. (Adapted from Deeny et al., (2009) with permission from Heldref Publications).

Taken together, the authors of these two studies suggested that these coherence results reflect a refinement of cortical networks in experts that was interpreted as a reduction of nonessential functional communications among the cortical regions of interest inducing in turn an improvement in motor performance. In other words, such coherence patterns provide brain biomarkers of specific motor planning as skill level increases allowing assessing the mastery level of a given task. As previously explained in the section related to the spectral power analysis, these studies assessed cortical dynamics for a well-established motor ability without addressing any learning manipulations of object or tool having unknown properties. As far as we know, only two investigations (Busk & Galbraith, 1975; Kranczioch et al., 2008) used coherence measurement to study learning during a visuomotor task. Specifically, Busk & Galbraith, (1975) reported decreased coherence between premotor (Fz) and motor (C3, C4) areas of the cortex and between the premotor and occipital regions, following practice on an eye–hand tracking task. More recently, Kranczioch et al., (2008) found changes in cortico-cortical coupling during learning of a visuomotor power grip tool. Specifically, they revealed that learning was variably associated with increased coherence between contralateral and/or ipsilateral frontal and parietal, fronto-central, and occipital brain regions. However, the learning period was relatively short (e.g., only the early learning stage was considered in Busk & Galbraith, (1975)) and these studies did not involve the suppression of familiar behavior used in the daily life.

By using the same tool learning protocol with unknown kinematics features (see section 3.1, Fig.6), a recent analysis (Gentili et al., 2009b) aimed to identify any changes in phase synchronization between two electrode pairs using both spectral coherence and PLV. The aim was to extract information from these measures to provide additional non-invasive functional brain biomarkers able to track the sensorimotor performance while subjects learned to manipulate a novel tool. The pre-processing of the EEG, the choice of the

frequency bands of interest and the kinematics processing were similar to that previously described in section 3.1 for the same tool learning task. Both the spectral coherence and the PLV have been computed as mentioned in section 2.3. A visual inspection of the data led us to consider a linear and a logarithmic model to fit the relationship between the spectral coherence/PLV changes and the kinematics parameters (MT, ML, RMSE) throughout learning. However, based on the criteria previously mentioned (see section 3.1), the logarithmic model allowed a better fitting of these relationships. It must be noted that, since for this experiment both spectral coherence and PLV provided similar results, thus, only the PLV results are presented in the following. The kinematics results are the same that those presented in section 3.1 (see Fig. 7A-C) indicating that the subjects learned to manipulate correctly the novel tool.

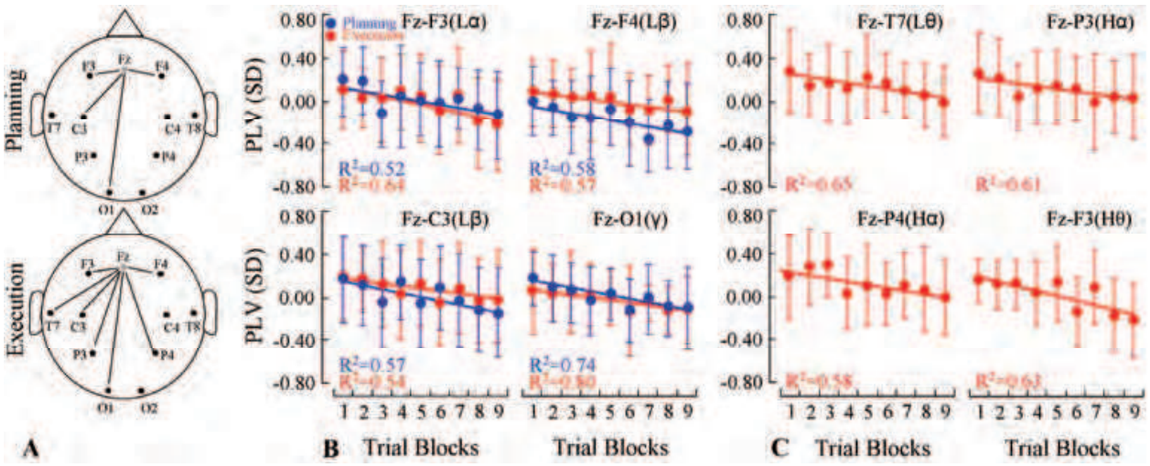


Fig. 13. Changes in PLV throughout the learning. A. Pair of electrodes showing a decrease of their synchronization throughout the learning during planning (top scalp plot) and execution (bottom scalp plot). B. Linear model capturing the changes in PLV during planning and execution for the pair of electrodes Fz-F3 (low alpha band), Fz-F4 (low beta band), Fz-C3 (low beta band) and Fz-O1 (gamma band). C. Linear model capturing the changes in PLV during execution for the pair of electrodes Fz-T7 (low theta band), Fz-P3 (high alpha band), Fz-P4 (high alpha band), and Fz-F3 (high theta band). (Panels A and B reproduced from Gentili et al., (2009b) with permission from IEEE).

While throughout learning the kinematics was enhanced (see Fig. 7A-C); electrophysiological changes in phase synchronization were simultaneously observed (Fig. 13A). Namely, as the subjects adapt, the electrodes pair Fz-F3 (low alpha band), Fz-F3 (low beta band), Fz-F4 (low beta band), Fz-C3 (low beta band) and Fz-O1 (gamma band) revealed a decrease captured by a linear model (i.e., $R^2 \geq 0.50$) for both movement planning and execution (Fig. 13B). For planning, the slopes of these linear models were significantly different from zero (t-test, $p<0.05$) for Fz-F3 (low components of the alpha and beta bands), Fz-C3 (low beta band), Fz-O1 (gamma band) and during execution for Fz-F3 (low alpha band) and Fz-C3 (low beta band) while a trend was observed for Fz-F3 (low beta band, $p=0.06$) and Fz-F4 (low beta band, $p=0.07$). Also, for execution, the same analysis revealed that the electrode pairs Fz-T7 (low theta band), Fz-P3 (high alpha band), Fz-P4 (high alpha

band) and Fz-F3 (high theta band) showed a significant linear decrease of the PVL (t-test, $p<0.05$) throughout adaptation (Fig.13C).
Such linear decrease was correlated with an enhancement of the performance and particularly good logarithmic correlations were found between the changes in phase synchronization and the MT and ML parameters. 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 logarithm ($R^2 \geq 0.40$) for both planning and execution. The same correlation analysis performed for the pairs Fz-T7, Fz-P3, Fz-P4, Fz-F3 and the MT and ML values revealed that the same results were obtained ($R^2 \geq 0.50$) only for movement execution.

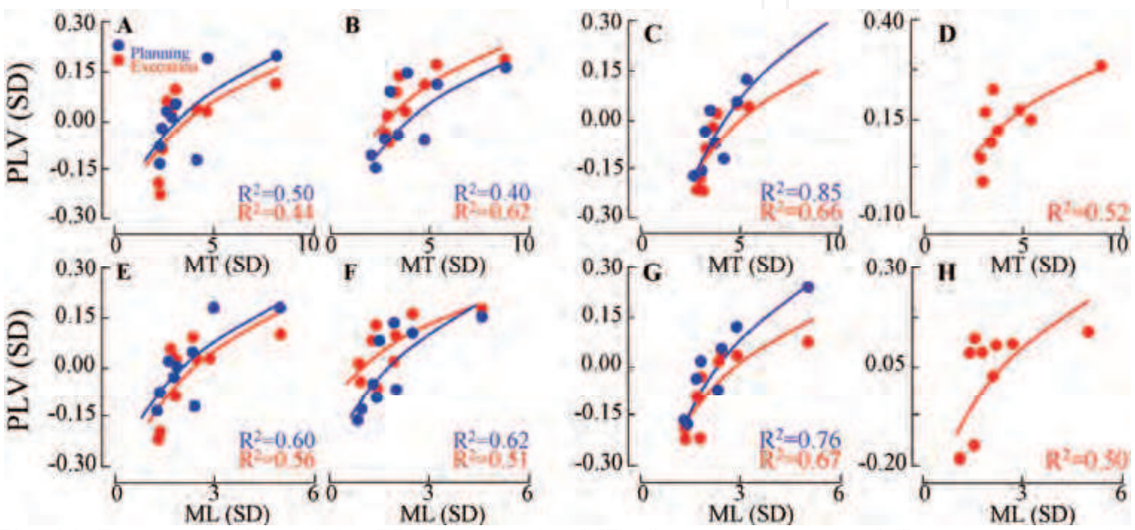


Fig. 14. Representation of the PLV versus the MT (first row) and the ML (second row) for both movement planning (blue color) and execution (red color). A. Pair Fz-F3 (low alpha band); B. Pair Fz-C3 (low beta band); C. Pair Fz-O1 (gamma band); D. Pair Fz-T7 (low theta band); E. Pair Fz-F3 (low alpha band); F. Pair Fz-C3 (low beta band); G. Pair Fz-O1 (gamma band); H. Pair Fz-F3 (high theta band). Since the Pair Fz-T7 (low theta band) and Fz-F3 (high theta band) revealed a non significant linear decrease during planning, the fits for PLV values versus MT and ML are only presented for execution (see panel D and H). (Panels A,B,E,F reproduced from Gentili et al., (2009b) with permission from IEEE).

As for the spectral power changes for the alpha and theta frequency bands, these changes in coherence/PLV presented above, allow assessing the level of performance but also its development throughout a learning period. Therefore, the spectral power and coherence/PLV provide brain biomarkers of the performance and learning in Human that may be useful in bioengineering/biomedical applications, particularly for brain monitoring applications and/or when the access to the actual performance is impossible. This will be presented in section 4, beforehand; the section 3.3 will present and discuss the advantages of these brain biomarkers but also their current limitations and the potential solutions to overcome them.

### 3.3 Strengths, weaknesses, and perspectives for brain biomarkers of the sensorimotor performance

#### 3.3.1 Strengths and weaknesses

By revealing correlations between the spectral power, coherence/PLV and motor performance, the research lines presented in this chapter provide potential non-invasive functional brain biomarkers to assess and track the level of performance and learning. It is important to note that these biomarkers are able to detect important differences in skills level such as those existing between novices and experts (e.g., Hatfield et al., 1984, 2004; Haufler et al., 2000) as well as to identify the learning dynamic related to different types of tasks inducing different neural resources (e.g., Gentili et al., 2008, 2009a,b; Kerick et al., 2004). Moreover, although their scalp locations and frequency band of interest present slight variations from one task to another, it appears that these biomarkers share also some frequency (e.g., alpha band) and spatial (e.g., temporal region) features while being located on specific electrodes for the various tasks tested. Therefore, beyond certain specificities that are task-dependent, these biomarkers of human performance share a common consistent topology in term of frequency and spatial scalp locations across different tasks. Moreover, it must be noted that changes in phase synchronization for a specific frequency range do not necessarily imply similar power changes for the same electrodes (Kiroi & Aslanyan, 2006). Therefore, the availability of processing techniques for extracting and combining both univariate (i.e., spectral power) and multivariate (i.e., spectral coherence/PLV) cortical measures might provide "multidimensional" brain biomarkers in the future. Such multidimensionality resulting from the combination previously described is expected to provide enhanced, robust biomarkers capable of tracking performance and learning dynamics, thus providing a potential solution to overcome limitations in current practical applications. This will be explained in the section 3.3.2.

Another important point is directly linked to the fact that these biomarkers were derived from EEG during movement execution, but, more importantly, during movement preparation (i.e., planning; Deeny et al., 2003, 2009; Gentili et al., 2008, 2009a,b; Hatfield et al., 2004; Haufler et al., 2000). The availability of these biomarkers during movement execution and particularly during movement preparation (i.e., planning) involves two specific advantages.

First, a biomarker of the performance during execution can be considered as a good complement of the behavioral measures available during and/or after movement execution. More importanty, the presence of these brain biomarkers during planning also allow estimating/predicting the on-coming performance level that is not available with usual peripheral and behavioral measurements. This important feature is common to many biomarkers such as the bispectral index derived from EEG used for the identification of anesthetic depth during pediatric cardiac surgery while the usual clinical signs are not accessible (Williams & Ramamoorthy, 2009).

Second, the availability of brain biomarkers of the performance during movement preparation is a feature that becomes particularly important when considering overt but, more importantly, covert movement executions in the context of bioengineering and biomedical applications for rehabilitation. The expression "overt movement execution" corresponds to a movement actually performed such as those executed in daily activities. In this case, the person can see and feel his/her own limb moving. Conversely, the term "covert movement execution", also commonly named mental or motor imagery, refers to a

dynamic mental process during which a subject internally simulates a motor action without activating the muscles and, therefore, without any apparent motion of the limbs involved in that action (Gentili et al., 2004, 2006; Jeannerod, 2001). Such motor imagery or covert execution is commonly used for mental practice/rehearsal of specific performance skills, BCI approaches and more generally in rehabilitation (see section 4 of this chapter). Interestingly, many studies revealed that common neurocognitive mechanisms in terms of both similar neural structures and behaviour exist between overt and covert motor actions (Fadiga & Craighero, 2004; Gentili et al., 2006; Jeannerod et al., 2001). In particular, several investigations suggest that motor imagery involves the same neural mechanisms as those activated during preparation (i.e., planning) and execution of overt movements (e.g., Jeannerod, 1994, 2001). Therefore, although our task involved actual movements, since the present results suggest that these brain biomarkers are accessible during movement preparation, they may also be suitable for covert movement execution when a task is performed using motor imagery.

Despite this research provided some interesting results and is still currently making progresses, two main limitations have to be considered. First, the present brain biomarkers of performance are based on a population analysis without considering subject individually. Second, their computation was based on the average value across several trials (e.g., 20 trials). Definitely, considering the variability of the MEG/EEG signals from one trial to another and also the sensitivity of the EEG signal to environmental noise and artefacts, the approach consisting in defining brain biomarkers of the performance needs to investigate, to what extent these results can be extended when single subject and single trials are considered. This is important for future applications since they will be designed for single subjects and ideally based on single or eventually few trials. Recently, by using MEG applied to a similar tool learning task (described in Fig. 6), we started to address these two problems by analyzing the alpha power band ([9-13Hz]) in individual subjects using the same ERD/ERS techniques and testing different sliding window (e.g., length, overlap) across trials. The preliminary results suggest that, at the individual level, the spectral power for the alpha band ([9-13Hz]) computed at the frontal, temporal and parietal regions during movement preparation were able to predict the motor performance (Gentili et al. 2009a).

### 3.3.2 Overcoming the current limitations by means of multiple constrains

As suggested in section 3.3.1, a possible way to overcome the two main limitations previously mentioned (i.e., single subject and computation based on single or few trials) is to obtain robust multidimensional EEG/MEG biomarkers able to assess the level of performance and learning by combining several individual biomarkers. In other words, the combination of several biomarkers would result in an increased number of conditions that have to be satisfied for estimating reliably any enhancement of the performance. The prediction problem is therefore constrained since a reliable estimation of performance needs to satisfy several constraints represented by the right combinations of biomarkers. For instance, if both a power increase and a coherence/PLV decrease are simultaneously observed for specific frequency bands and brain regions, it seems reasonable to predict with a certain confidence that the subjects are successfully learning the task. Conversely, if we would have only one biomarker, this prediction would be less reliable. Therefore, the combination of several brain biomarkers such as phase synchronization and spectral power would provide cross-information resulting in the generation of robust and accurate non-

invasive brain biomarkers of the motor performance. This approach could also give insight into possible reasons for the failure of sensorimotor learning and adaptations. Thus, such multidimensional brain biomarkers might be better suited for applications based on individual subjects and single or few trials.

It must be noted that, this first type of constraint was related to a combination of various biomarkers using the same brain imaging modality, i.e., EEG/MEG signals. However, another type of combination could also be considered by using the fusion across multiple recoding modalities in order to complement information provided from each imaging technique. For instance, in order to complement EEG/MEG signals analysis, fNIRS signals processing could provide additional brain biomarker by measuring the hemodynamic of brain activity. The choice to use fNIRS is guided by three reasons: First, although the hemodynamic activity has a lower temporal resolution than EEG, the fNIRS potentially provides more direct spatial resolution or localization abilities over EEG (Soraghan et al., 2008). Thus, with the superior temporal resolution of EEG, merging these two techniques would allow for "the best of both worlds" (Coyle et al., 2007). Second, contrary to EEG, the hemodynamic response is influenced by head/body orientation with respect to the gravitational axis whereas fNRIS signal is relatively less sensitive to artefact and environmental noise than EEG. Once again, since both do not have these two common weaknesses their combination appears to be advantageous. Third, although fNIRS only penetrate the cortex relatively superficially (~2.0 cm; Rolfe, 2003) contrary to classical fMRI, these signals can be recorded by portable devices as it is also the case for EEG, making them, particularly well suited for applications in practical/ecological situations with various populations (e.g., healthy persons, patients, children, elderly, military personnel, etc.). It must be noted that the idea to combine several biomarkers within (power, coherence/PLV) and between (fNIRS) imaging modalities has already been proposed for clinical applications (Guarracino et al., 2008) such as for brain injury prediction (Ramaswamy et al., 2009) and amyotrophic lateral sclerosis (Turner et al., 2009). From a practical point of view, this signal fusion across multiple imaging modalities could ideally be performed by using a recoding system that embed both EEG and fNIRS sensors.

### 3.3.3 Emotional states on brain biomarkers of the performance

A question that is naturally raised is the influence that some psychological and mental states such as emotion, stress or fatigue could exert over the quality of sensorimotor performance. If such adverse psychological and mental states disrupt the motor performance, it is legitimate to wonder to which extent the biomarkers tracking this same performance would also be affected. However, the majority of the performance stress-related studies focus on behavioural aspects without analyzing the cortical dynamics (Staal et al., 2004). Ongoing research by Hatfield and colleagues is beginning to provide some insight into such questions by placing performers under stressful conditions. For instance, Rietschel et al., (2008) asked participants to perform a marksmanship task under both regular performance-alone and competitive conditions. Changes in the Spielberger State Anxiety Inventory (STAI), heart rate, cortisol and skin conductance evidenced an increased state anxiety during the competitive condition. Furthermore, the performance was affected during the competition along with a significant decrease in alpha power. Similarly, when subjects performed a drawing movement task under high level arousal conditions they exhibited higher levels of coherence associated with decreases in performance (Rietschel et al., 2006).

Therefore, these results provide evidence that the brain biomarkers of sensorimotor performance can be disrupted by psychological and mental states such as emotion, stress. Thus, from a physiological point of view, it is possible to consider that an increased degree of stress would induce the recruitment of nonessential neural resources during task execution, leading to a reduction of cortical refinement (i.e., a reduction of alpha power and an increase in cortico-cortical communication) that reflects sub-optimal performance. In other words, we could consider that, to some degree, the brain biomarkers are contaminated with a sort of noise. However, even in this case, they may still be informative since in some instances they could also unravel the possible causes (e.g., stress, fatigue) of alterations in behavioral performance which cannot be revealed by peripheral motion parameters (e.g., kinematics) alone. For instance, in the study where subjects learn a novel tool, the absence of learning/adaptation could also be due to fatigue. Nevertheless, when considering the spectral power, the frontal biomarkers evidenced here are neither in the same spatial location (frontal midline) nor in the same frequency band (low theta band) than the fatigue-related EEG power (Makeig et al., 2000; Oken et al., 2006). Similarly, when considering the coherence/PLV, factors such as stress or fatigue imply an increase and not a decrease in phase synchronization and is generally identified for different electrodes pairs and/or frequency bands (Andersen et al., 2009; Lorist et al., 2009) than those found in the tool learning study (see section 3.2). Therefore, this clearly illustrates: i) the advantage to combine different biomarkers of the performance to obtain more robust predictions, ii) the benefit to combine them with other biomarkers identifying some adverse mental states (e.g., fatigue, stress) to be able to better decipher or indicate potential causes of a poor learning performance. Futures research should provide insights about these various possibilities, their benefit and limits.

### 3.3.4 Fusion of structural and functional brain biomarkers

Although the two previous sections (3.3.2 and 3.3.3) focused on different problems, both of them emphasized the importance for cross-information by combining several biomarkers. Indeed, it can be reasonably expected that such combination of biomarkers would lead to a robust tracking of motor performance and learning. It must be noted that such a combination can be performed not only between functional biomarkers but also between both structural and functional biomarkers. For instance, biomarkers can predict the performance based on information at the genetic/molecular level (e.g., naloxone, cortisol) or from behaviour such as heart rate or skin conductance (Armstrong & Hatfield, 2006). Thus, such convergence between these biomarkers, different in nature, would allow performing an even more robust prediction to assess accurately the level of performance and to track/predict precisely the learning dynamic. Although this chapter introduced mainly the concept of functional brain biomarkers for performance assessment, it appears clearly that both structural and functional brain biomarkers must be seen as a complementary source of information. Interestingly, while structural brain biomarkers using methods form genetic may be more appropriate on a long timescale prediction such as very early diagnostic, functional biomarkers may be better suited for short timescale prediction such as a real-time tracking of the neural events. Such combination of structural and functional brain biomarkers is an emerging research line. For instance, recently Deeny et al., (2008) investigated MEG measurements in relation to genetic markers such as the epsilon4 allele of

the apolipoprotein, providing a method to detect risk factors for Alzheimer's disease (Corder et al., 1993).

## 4. Current Brain Biomarkers for Sensorimotor Performance and Bioengineering Applications

Beyond the considerations presented in section 3, the techniques presented to record and process brain biomarkers non-invasively using portable systems make them particularly well suited for real-time (or close to real-time) prediction in practical/ecological applications. Although multiple potential applications can be considered for the future, this section will illustrate two possible applications. The first one will be the design of future smart neuroprosthetics by proposing solutions to overcome some well-known BCI-related problems. The second application (that is actually to some extent a generalization of the first one) will be related to brain monitoring in the context of overt and covert movement execution to accelerate learning or re-learning when a task is performed/learned using actual movements and/or motor imagery.

### 4.1 Neuroprosthetic applications: towards a smart Brain Computer Interface

The changes previously described in EEG power and coherence/PLV that mirror human motor performance may potentially provide powerful biomarkers for tracking human learning/adaptation status when one has to learn/adapt to a new tool. A first potential interesting role of these brain biomarkers would be to overcome the well-known difficulties related to BCI systems such as adaptive decoding, constant recalibration and the maintenance of stable performance while a user tries to control a neuroprosthesis (Vaughan et al., 2003). Traditionally, motor-imagery-based BCI approaches are divided into two phases. The first one consists of a calibration phase to determine the parameters of a decoding algorithm, which has to map neural signals to a class of imagined movement. The second phase aims to train the subject by providing him/her sufficient feedback to change his/her cortical dynamics in order to control an external device via the BCI system. It is important to note that during this second stage, since the adaptation depends on the capacity of the user's brain to change its cortical dynamics, frequent recalibrations of the decoding algorithms are required when the user's performance degrades (Blankertz et al., 2009). In order to address these problems, some solutions have been proposed and notably by means of adaptive algorithms (Blankertz et al., 2006; Sykacek et al., 2004). However, these approaches use supervised adaptation based on *a priori* knowledge of an external target. Although helpful, the requirement of such *a priori* information actually represents a major pitfall for practical BCI applications since the user should decide when and where to direct his/her intentions. In other words, no information of external targets is available to the decoding algorithm (Blankertz et al., 2006; Vidaurre et al., 2007). The complexity of using two adaptive controllers (the user's brain and the decoding algorithm) is not new and has been already raised (McFarland et al., 2006; Vaughan et al., 1996); however, it continues to be an issue, and no satisfying solutions of this problem have been provided (McFarland et al., 2006). The brain biomarkers of performance presented in this chapter may help to overcome such important drawbacks of BCI. Indeed, such biomarkers could be used to continuously adapt the decoding algorithm to the subject's mental states, thereby allowing a stable co-adaptation/cooperation between the user and the BCI system. This is especially

relevant when the user has to learn the physical properties of a new tool and/or a novel environment as is the case when a user intends to control a neuroprosthetic device. For example, the alpha power at the frontal, temporal and parietal sites combined with coherence/PLV for the low beta frequency bands between the pair of electrodes Fz-F3 and Fz-C3 could be computed using a sliding window (e.g., 15-20 trials). If the user's brain considerably adapts as indicated by an increased alpha power combined with a reduced coherence/PLV at the brain sites mentioned above, then the BCI decoding algorithm should not update its parameters. Conversely, it should adjust the parameters, by using, for instance, a reinforcement learning signal, to compensate for a user's poor performance (in that case reflected by a decreased alpha power and an increased coherence/PLV at the brain sites mentioned above).

As previously mentioned in section 3.3.3, the use of such biomarkers could also reveal the sources of alteration in behavioral performance which cannot be revealed by kinematics parameters alone. For instance, poor learning/adaptation performance could be due to other factors such as stress or fatigue. These biomarkers, thanks to their specificities in term of scalp sites and frequency bands (and also with eventual additional information such as hemodynamic response provided by fNIRS), could reasonably unravel the possible origin of poor motor learning, providing, therefore, relevant covert supervision of the user during BCI training. For example, in practical use, it is important to decipher if a user's poor BCI performance is related to fatigue or to bottlenecks related to information processing guiding the algorithm to adapt to the user's cognitive state, which is usually impossible to access from behavior.

### 4.2 Brain monitoring applications

Another possible application of functional brain biomarkers would be related to brain monitoring for overt and more importantly for covert execution. It is well known that motor imagery, or covert execution, share a lot of functional commonalities and that many neural structures are commonly activated during both overt and covert movement. On the other hand, there is also a growing body of evidence that suggests that it is possible to learn, or at least improve, performance with practice using motor imagery also called mental training. Most of the studies focusing on mental practice either considered performance enhancement in a healthy population (e.g., Gentili et al., 2006; Yaguez et al., 1998) or a rehabilitation (e.g., Jackson et al., 2004; Page et al., 2001) context where a positive effect on subsequent actual motor performance was evidenced. While it is possible to assess the effects of such covert practice on subsequent actual movements, it is impossible to continuously monitor mental training (unless a trial is actually executed) since no overt execution is available. However, the brain biomarkers presented here would allow for assessing the level of performance during mental training and tracking of learning dynamics. Such brain biomarkers could be coupled to a neurofeedback system providing, thus, an enhanced feedback of performance during overt execution (in addition to classical feedback) or covert execution where usually no feedback is available. Such brain monitoring systems for covert/overt movement execution would allow efficient supervision of performance, resulting in an accelerated learning or re-learning. Such bioengineering systems could be applied in various populations ranging from military personnel desiring to rapidly acquire skills to any persons subjected to a motor impairment undergoing rehabilitation where enhanced guidance for both patient and therapist would be beneficial. It must be noted that these

biomarkers would allow monitoring and fitting of the training time-scale for each individual since it is reasonable to expect that two individuals will not mentally learn at the same speed. For instance, for the same task some individuals using mental practice may need 40 trials to reach acceptable performance while others would need 60 trials to reach the same level of performance. However, it is not possible to detect any progression in performance when using motor imagery (except by occasionally using actual execution) unless we use these brain biomarkers to create a customized training timescale for each individual. Moreover, as for BCI application, it would also be possible to know if a poor performance is related to sensorimotor learning processes or induced by some adverse mental states such as fatigue. Thus, the therapist could adapt the current rehabilitation session to the patient's cognitive state in order to improve training efficiency without having to access behavioral measures.

At present, the current research focuses mainly on brain biomarkers for healthy people since a well-established model of these brain biomarkers needs to be defined before moving towards practical applications for pathology in a rehabilitation context. It is of interest to consider if such brain biomarkers would be applicable for patients subjected to neural pathologies. Although these biomarkers should be affected by a given pathological state, it is still possible to find their modified version adapted to this pathology as a BCI decoding algorithm is able to map a pathological neural activity to the desired output (Neuper et al., 2003). This would necessitate applying the same techniques and approaches, albeit with some modifications, to provide biomarkers engineered for specific neural pathologies. For instance, it has been suggested that mental imagery practice would have positive effects on persons subjected to cerebral palsy (Trusceli et al., 2008; Zabalia, 2002). Therefore, under such conditions, the cerebral palsy-specific performance biomarkers would allow monitoring of the brain to provide feedback for a therapist in order to accelerate and improve performance and, thus, the physical therapy process. It must be noted that, beyond application, such brain biomarkers could also provide useful information about the cortical neural networks of patients suffering from neural diseases. Still taking the example of patients with cerebral palsy, specifically, these brain biomarkers could provide insights into the effects of physical therapy by, for instance, estimating the benefit of motor imagery on reorganization of cortical dynamics and the degree of automatization of the movement. Namely, the coherence/PLV biomarker (Busk & Galbraith, 1975; Deeny et al., 2003, 2009; Gentili et al., 2009b) may be of particular interest to analyze any possible changes in cortical network recruitments throughout the rehabilitation procedure associated with any potential motor performance improvement. Moreover, several investigations have suggested that an increase in alpha power in the temporal, frontal regions would reflect that movement become more automatized as a function of practice, requiring less attentional and processing resources, since as strategies and skills are developed, there is a less extensive cortical contribution to task performance, resulting in increased alpha power (Gentili et al., 2008, 2009a; Hatfield et al., 2004; Smith et al., 1999). Therefore, when using mental imagery the computation of such spectral power could provide a biomarker able to assess the degree of automatization of the repeated actions throughout a rehabilitation session. Finally, as previously mentioned, a multidimensional brain biomarker could be even more effective by combining information such as the spectral power, coherence/PLV and hemodynamic responses using fNIRS.

## 5. Conclusions and Perspectives

Nowadays, some non-invasive functional brain biomarkers able to assess cognitive-motor/sensorimotor performance and learning level are available. However, they were mainly analyzed by means of investigations based on populations of subjects. The next challenge is to generalize these biomarkers to single subjects using single or few trials in tasks using actual movements or motor imagery. In order to reach these new aims, further research is needed to provide multidimensional biomarkers by considering the fusion of both processing techniques (e.g., EEG/MEG spectral power and coherence) and the nature of neural signals (e.g., hemodynamic response with fNIRS). Such approaches are expected to provide robust models for these biomarkers. Today, these brain biomarkers are engineered based on healthy people; however, in the future these methods could be transferred to alleviate neural disorders, provide new types of smart neural prostheses, and create brain monitoring tools to allow the emergence of a new generation of assistive technology for both healthy (e.g., accelerated learning) and pathological (e.g., rehabilitation) human populations.

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## 7. References

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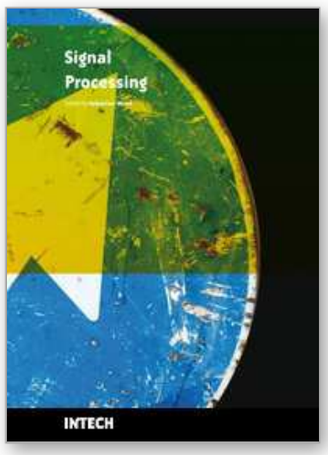


**Signal Processing**

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This book intends to provide highlights of the current research in signal processing area and to offer a snapshot of the recent advances in this field. This work is mainly destined to researchers in the signal processing related areas but it is also accessible to anyone with a scientific background desiring to have an up-to-date overview of this domain. The twenty-five chapters present methodological advances and recent applications of signal processing algorithms in various domains as telecommunications, array processing, biology, cryptography, image and speech processing. The methodologies illustrated in this book, such as sparse signal recovery, are hot topics in the signal processing community at this moment. The editor would like to thank all the authors for their excellent contributions in different areas of signal processing and hopes that this book will be of valuable help to the readers.



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