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Motor state transitions and Breathing in Brain Machine Interfaces

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Inspiration is not an idea, inspiration is not the ability to do certain things, but inspiration is everything that surrounds us: our environment, the people that exist on this earth and what we experience on a daily basis whether it is good or bad. — Anonym

To Pauline, the person who inspired this thesis...

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B. O.

Abstract

Brain-Machine interfaces aim to create a direct neural link between user's brain and machines. This goal has pushed scientists to investigate a large spectrum of applications in the realm of assistive and rehabilitation technologies. However, despite great progress, the possibility of being in full control of a device with our brain is still far to be reached.

One of the primary limitations of BMIs is the notion of self-paced control, which states that a user should be able to activate or deactivate such interface by mere modulation of brain activity. Many studies have investigated this question, focusing notably on the use of endogenous signals (such as Event-Related Desynchronization/Synchronization, ERD/S) to control the activation of these interfaces in natural interaction scenarios. This question is, however, largely ignored when looking at their interruption. Hence, in this first part of the thesis, my work was devoted to investigating how a BMI user would be able to control the interruption of noninvasive BMIs based on Motor Imagery (MI), a paradigm promoting natural and endogenous signals that can be used for BMI control. I investigated the decoding of motor termination as well as its correlates characterized by the post-movement ERS phenomenon. Specifically, this part of the thesis aimed to study (i) the feasibility to decode motor termination from a specific neural correlate as well as the adaptation from the user in closed-loop scenarios, (ii) the benefits of using motor termination correlates to detect the stopping process, and (iii) the effect of BMI effectors such as an exoskeleton on the detection of motor termination correlates. The obtained results provide new insights into closed-loop decoding of motor termination. In particular, I show that BMI users exhibit an adaptation of their EEG correlates enabling them to have a reliable control when switching off a BMI in closed-loop scenarios. Second, I show that the decoding of motor termination is a particular process different from a resting state and, hence, should be decoded independently so as to achieve a faster and more robust detection. Finally, I investigate the use of BMI effectors with respect to the decoding of motor termination showing an effect of the effectors on the correlates of motor termination. However, due to the nature of these correlates, motor termination can still be reliably decoded with a similar latency.

In the second part of my thesis, I also investigate how the interoceptive system affects BMI

and particularly how breathing signals affect BMI based on MI. Breathing has been shown to have a key effect on numerous human functions, including, perceptual, cognitive, and motor functions. However, currently not much is known about the role of respiratory signals in BMI and such signals have rather been considered as physiological noise. In my thesis, I evaluated how the breathing process affects the correlates of MI (ERD in μ and β bands) as well as actual BMI performance. The results provide an extensive analysis regarding the effect of the breathing cycle specifically on μ -ERDs, showing stronger ERD during the late expiration phase. Moreover, I identified a link between breathing and BMI performance and propose that breathing signals are valuable predictors for BMI performance highlighting the importance of monitoring such signals and, more generally, presenting the interoceptive system as a key component of motor preparation and motor imagery.

Keywords Brain-Machine Interface, Electroencephalogram, Motor imagery, Motor termination, Breathing.

Résumé

Les interfaces cerveau-machine (BMI) visent à créer un lien neural direct entre le cerveau de l'utilisateur et les machines. Cet objectif a poussé les scientifiques à étudier un large éventail d'applications dans le domaine des technologies d'assistance et de réhabilitation. Cependant, malgré les grands progrès réalisés dans ce domaine, le contrôle total d'un appareil avec notre cerveau est encore loin d'être atteint.

L'une des principales limites du BMI est la notion de contrôle autonome, qui stipule qu'un utilisateur doit pouvoir activer ou désactiver une telle interface par simple modulation de son activité cérébrale. De nombreuses études se sont penchées sur cette question, en se concentrant notamment sur l'utilisation de signaux endogènes (tels que la désynchronisation/synchronisation liée à un événement, ERD/S) pour contrôler l'activation de ces interfaces dans des scénarios d'interaction naturelle. Cette question est toutefois largement ignorée lorsqu'on examine leur interruption. C'est pourquoi, dans cette première partie de la thèse, mes travaux ont été consacrés à l'étude de la manière dont un utilisateur du BMI serait capable de contrôler l'interruption de BMI non-invasives basées sur l'imagerie motrice (MI), un paradigme favorisant les signaux naturels et endogènes qui peuvent être utilisés pour le contrôle des BMIs. Pour ce faire, j'ai étudié le décodage de la terminaison motrice ainsi que ses corrélats caractérisés par le phénomène ERS post-mouvement. Plus précisément, cette partie de la thèse visait à étudier (i) la faisabilité du décodage de la terminaison motrice à partir de corrélats neuraux spécifique ainsi que l'adaptation de l'utilisateur dans des scénarios en boucle fermée, (ii) les avantages de l'utilisation des corrélats de terminaison motrice pour détecter le processus d'arrêt, et (iii) l'effet des effecteurs BMI tels qu'un exosquelette sur la détection des corrélats de la terminaison motrice. Les résultats obtenus apportent de nouvelles connaissances sur le décodage en boucle fermée de la terminaison motrice. En particulier, je montre que les utilisateurs de BMI présentent une adaptation de leurs corrélats EEG leur permettant d'avoir un contrôle fiable lors de la désactivation d'un BMI dans des scénarios en boucle fermée. Deuxièmement, je montre que le décodage de la terminaison du moteur est un processus particulier différent d'un état de repos et, par conséquent, devrait être décodé indépendamment afin d'obtenir une détection plus rapide et plus robuste. Enfin, j'étudie l'utilisation des effecteurs BMI pour le décodage de la terminaison du moteur, en montrant l'effet des effecteurs sur les corrélats de la terminaison du moteur. Cependant, en raison de la

nature de ces corrélats, la terminaison motrice peut encore être décodée de manière fiable avec une latence similaire.

Dans la deuxième partie de ma thèse, j'étudie également comment le système intercepteur affecte le BMI et en particulier comment les signaux respiratoires affectent le BMI basé sur de la MI. Il a été démontré que la respiration a un effet clé sur de nombreuses fonctions humaines, y compris les fonctions perceptuelles, cognitives et motrices. Cependant, le rôle des signaux respiratoires sur le BMI est actuellement méconnu avec ces signaux plutôt considérés jusqu'à maintenant comme un bruit physiologique. Dans ma thèse, j'ai évalué comment le processus respiratoire affecte les corrélats de BMI (ERD dans les bandes μ et β) ainsi que les performances réelles du BMI. Les résultats fournissent une analyse approfondie concernant l'effet du cycle respiratoire spécifiquement sur les ERDs de μ , montrant des ERDs plus forts pendant la phase d'expiration tardive. De plus, j'ai identifié un lien entre la respiration et la performance du BMI et je propose que les signaux respiratoires soient un prédicteur précieux de la performance du BMI, soulignant l'importance de surveiller ces signaux et, plus généralement, je présente le système intéroceptif comme un élément clé de la préparation motrice et de l'imagerie motrice.

Mots-clés Interface Cerveau-Machine, Electroencéphalographie, Imagerie motrice, Terminaison motrice, Respiration

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1 Introduction

The ability to communicate or move can be severely impaired as a result of traumatic brain injury and is often seen after a stroke or spinal cord injury. Such traumatisms leads to a significant deterioration of quality of life and imposes physical and psychological barriers around those who survived. In response to such damaging circumstances, an emerging solution is the use of Brain-Machine Interfaces (BMIs). BMIs aim at providing communication and control solutions for people with motor disabilities (Millán et al., 2010) by bypassing impaired neural pathways. Because it is currently one of the few solutions still holding promises for such patients, BMI research has witnessed an impressive expansion in the last few years and has pushed scientists to investigate a large spectrum of applications in the realm of assistive and rehabilitation technologies.

Two major types of BMIs are recognized based on the degree of invasiveness required to record brain activity: *invasive* and *non-invasive* BMIs (Lebedev and Nicolelis, 2006). *Invasive* BMIs rely on invasive methods through intracranial electrodes allowing signal acquisition recorded directly in the brain at the level of an individual neuron (single units) or multiple neurons (multi-units, local field potential). Thus, they result in a good Signal-to-Noise ratio (SNR) with high resolution signals required to address complex problems with multiple degrees of freedom. Unlike invasive BMIs, non-invasive BMIs record brain activity through scalp electrodes avoiding any brain surgery. This advantage comes unfortunately with a much lower spatial resolution and a higher Signal-Noise Ratio (SNR). Still, the efficacy of non-invasive BMIs has been demonstrated many times in the control of external devices such as spellers (Birbaumer et al., 1999; Perdikis et al., 2014), avatars (Perdikis et al., 2018), telepresence robots (Leeb et al., 2015), wheelchairs (Galán et al., 2008; Iturrate et al., 2009) or hand prosthesis (G. R. Müller-Putz, Scherer, Pfurtscheller, et al., 2005; Tavella et al., 2010).

While some of these BMIs are based on a voluntary response to an external stimulus (*exogenous* signal), a large majority of BMIs aims also to facilitate the control by relying on a more natural and intuitive interaction between the machine and the user using neural signal that can be naturally elicited by the user (*endogenous* signal). In this context, self-modulation of brain activity through Motor Imagery (MI) task – where users imagine movement of differents

part of their body (hands, feet, tongue, ...) – has been widely employed as a paradigm to control BMI. However, while these BMIs exploit the decoding of movement initiation (Lew et al., 2012; G. R. Müller-Putz, Scherer, Pfurtscheller, et al., 2005; Niazi et al., 2011; Tavella et al., 2010), the decoding of movement termination has been rather ignored (Rae et al., 2014; Schultze-Kraft et al., 2016). Consequently, the "stop" signal is only obtained indirectly when the neural correlates of MI are no longer identified. Although the detection of movement initiation is critical in the process, decoding the volitional interruption of a movement is of equal importance to endow brain-actuated devices with more natural behavior. Beyond the interruption control per se, adding this module may bring finer control of BMI effectors (e.g. hand orthosis, functional electrical stimulation) such as the control of the grasping level. In line with this, several studies have shown that maintaining continuous control of devices such as an exoskeleton constitutes a major challenge in the field (Soekadar et al., 2016).

Following the need for finer control of BMI effectors, in my thesis I studied EEG correlates of motor imagery while considering MI not as a sustained motor task but rather on its motor state transitions that distinguish initiation (MI onset) and termination (MI offset). My goal was to investigate how MI-based BMIs can benefit from the decoding of these motor state transitions compared to the state-of-the-art approach. In addition, I also investigated how physiological signals such as respiratory signals impact MI-based BMIs by looking at the effect of breathing on the correlates of these motor state transitions as well as the BMI performances.

The rest of this introductory chapter presents the concepts and themes that I use in this thesis. In the following sections, a brief overview of the field of BMI is given and notably on the MI-based BMIs and their principles. Then, I focus on the movement termination and the current existing BMIs called Beta-rebound based BMIs as well as the use of breathing signals in BMIs. Finally, I present the structure of the thesis introducing the contents as well as a summary of the results for each chapter.

1.1 Non-invasive BMIs

To enable the translation of user intentions into commands for external devices, several elements can be listed as key components of BMIs (see Fig. 1.1).

Signal acquisition - Most non-invasive BMIs rely on the interpretation of electroencephalography (EEG) signals. These signals are thought to be primarily generated by cortical pyramidal neurons in the cerebral cortex that are oriented perpendicularly to the surface of the brain. Hence, with an EEG composed of multiple electrodes laying along the scalp, one can record the neural activity (Pfurtscheller, 2001; Pfurtscheller and Lopes Da Silva, 1999) corresponding to the summation of millions of neurons firing in synchrony with changes that can be monitored with an impressive temporal precision (in the order of milliseconds).

Feature extraction and selection - To increase the Signal-to-Noise ratio (SNR), diverse preprocessing techniques such as spatial and temporal filtering are generally applied to EEG signals

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(Blankertz, Tomioka, et al., 2007). After that, the step of Feature Engineering can take place in the process with this last aiming to extract and select relevant attributes (i.e. features) which characterize the brain state of interest. Here, methods such as Fourier transform (Al-Fahoum and Al-Fraihat, 2014), autoregressive model (McFarland and Wolpaw, 2008; Zhang et al., 2017) or Common Spatial Pattern (Ang et al., 2008; Thomas et al., 2009) are generally reported in the literature.

Classification - A decoder based on these features is then built and is designed to determine the current brain state of the user. These decoders are usually based on machine learning algorithms and aim to classify between several brain states (i.e. classes). Classification algorithms are usually categorized in three main categories: linear classifiers, non-linear classifiers, or deep neural networks. While non-linear classifiers and deep neural networks are still less common, linear classifiers such as Linear Discriminant Analysis or Support Vector Machine are widely spread in the field and preferred for online and real-time BMIs (Lotte et al., 2018; Lotte et al., 2007). Metrics from the field of machine learning such as the accuracy, the Area Under Curve (AUC) or the Receiver Operator Characteristic (ROC) are usually used as metrics to quantify and evaluate the BMI performances of such a decoding.

BCI Feedback - The likelihood of this decoding is finally post-processed (e.g. probability smoothing) and transformed into a visual, auditory, or proprioceptive feedback informing the user of his real-time performance (closed-loop feedback). This feedback allows the user to learn the correct way to modulate his brain signals and to acquire BMI skills necessary to send commands and control a device.



Figure 1.1 – Main Component of a typical closed-loop BMI system. Main Component of a typical closed-loop BMI system which includes the acquisition of the signal based for a non-invasive recording method such as an electroencephalogram (Signal Acquisition). The signal obtained is often preprocessed with filter methods. Features are extracted (Feature Extraction) from this signal and are assigned to a specific brain state. Using only relevant features (Feature Selection), a decoder is built to identify and discriminate between different brain states (Classification). The output of such a decoder is then processed (Post-Processing) and translated into feedback (BCI Feedback) and promotes the learning of the user (Subject) to deliver commands and control the device (Device). The figure was taken from Perdikis, 2014.

1.2 Endogenous non-invasive BMIs

EEG-based BMIs are commonly relying on a specific signal recorded from the brain activity in a given paradigm. These signals can be either a voluntary response to an external stimulus exploited in *exogenous* BMIs or either self-generated response through mental tasks for *endogenous* BMIs (McFarland and Wolpaw, 2008; Wolpaw et al., 2002). Among exogenous signals, we can notably find the Visual Evoked Potentials (Spehlmann, 1965) as well as the Event-Related Potentials with this last category englobing those based on the P300 component (Fabiani et al., 1987) and on Error-related potentials (Schalk et al., 2000). These signals have been extensively studied and were successfully used for computer games (Chen et al., 2017),

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spelling devices (Farwell and Donchin, 1988; G. R. Müller-Putz, Scherer, Brauneis, et al., 2005) or external devices such as wheelchair control (Iturrate et al., 2009). Despite these results, exogenous BMI systems may suffer from critical limitations which prevent them for being daily use. Indeed, those systems are built in such a way that they require a permanent attention from the user since a constant flow of stimuli is received in order for him to make a decision. Hence, fatigue and system dependency are major drawbacks of such systems which can be then seen as independent of the user's choice and his will to use it voluntarily.

On the contrary, because endogenous signals can naturally be elicited, these signals are ideally suited candidates for being used in BMIs on a daily basis. Here, one popular approach relies on the changes in brain rhythms during the planning and execution of movements that can be observed and recorded through non-invasive techniques such as EEG. Importantly these changes can also be observed when the movement is only imagined since motor imagery (MI) is closely related to the planning phase of a movement. Following such changes in brain activity, different motor correlates have been investigated and used as endogenous signals to control BMIs. Particularly the use of neural correlates of movement onset based on low-frequency rhythms (movement-related cortical potentials, MRCPs) and sensorimotor rhythms (SMRs) have been extensively studied.

Movement-related cortical potentials - MRCP are slow event-related direct-current shifts (f < 3Hz) of the EEG signal. This signal is made of two main components. The first component can be described as a slow negative potential starting 1.5 s before a voluntary movement (i.e. readiness potential, RP). This negativity is more prominent over the central-medial scalp and presumably originates in the Supplementary Motor Area (SMA) as well as primary motor cortex (M1) (Wildgruber et al., 1997). The second component occurs 400 ms before movement and is characterized by a steeper slope over the contralateral primary motor area (Shibasaki and Hallett, 2006). These slow rhythms originate from depolarizations of the apical dendritic tree in the upper cortical layers caused by synchronous firing, mainly from thalamocortical afferents, showing local excitatory mobilization for negative slow potentials (Birbaumer, 1999). Initially applied in BMI speller (Kübler et al., 2001), MRCPs have been principally used for movement onset detection in closed-loop BMI for rehabilitation (Lew et al., 2012; Mrachacz-Kersting et al., 2012; Xu et al., 2014).

Sensorimotor rhythms - Representing the dynamics of brain oscillations, SMRs are timelocked to triggered events and can be naturally elicited in a self-paced way. SMRs do not necessarily depend on motor cortex output or any muscle activation. The presence of these rhythms was reported in movement imagery (Schlögl et al., 2005), passive movements (G. R. Müller-Putz et al., 2007) as well as in action observation (Babiloni et al., 2002). SMR were also used as a communicative tool with spelling systems such as Hex-o-Spell (Blankertz et al., 2006) or Brain Tree (Perdikis et al., 2014). These patterns were used as well in the decoding of motor intention and combined with BMI effectors such as robotic orthosis (Ramos-Murguialday et al., 2013) or functional electrical stimulation (FES) (Biasiucci et al., 2018; Pfurtscheller, Müller, et al., 2003).

1.3 SMR-based non-invasive BMIs

As mentioned above, movement imagination is closely linked to the preparation of movement and can elicit SMR patterns comparable to those when executing a movement. A SMR attenuation is usually called an Event-Related Desynchronization (ERD) and is explained by an increase of excitability of cortical neurons or activated cortical neurons. The opposite effect, an amplification of SMR is called an Event-Related Synchronization (ERS) and is explained by a decrease of excitability of cortical neurons or inhibited cortical network neurons (Pfurtscheller, 2001; Pfurtscheller and Lopes Da Silva, 1999). These patterns are characterized by two main features: frequency and topographically.

First, these patterns can be characterized by their frequency. For example, when performing hand MI, an ERD is generally expected in μ band (8-12Hz) as well as in β band (13-30 Hz) (Pfurtscheller et al., 2006) while an ERS is expected in the β band when performing feet MI. Additionally, these patterns usually follow a specific spatial characterization and are based on the homunculus representation (i.e. a distorted representation of the human body based on the map of brain areas dedicated to motor or sensory processing for different anatomical divisions of the body) (Penfield and Boldrey, 1937). Based on this, different topographic patterns can be expected when performing different MI tasks. For example, during hand MI, an ERD can be observed in the hand area over the contralateral cortex (right hand – channel C3, left hand – channel C4) while during foot MI, an ERS is expected in the cortical foot area (central channel Cz). Although both spatial and frequency characterization constitutes a prior knowledge, it is worth to note that these characteristics can change between subjects.

To promote and exploit ERD/ERS patterns, most non-invasive BMIs are basing their systems on Motor Imagery (MI) paradigms where people are asked to mentally rehearse a given motor activity without any overt motor output (Decety, 1996). In this paradigm, two main types of MI can be differentiated. In visual imagery (VI), the person is asked to rehearse the movement and visualize it. In kinesthetic imagery (KI), the person is asked to rehearse the movement and focus on the bodily sensations associated with movement execution. Because of clearer patterns and better performance, the latter is usually preferred (Neuper et al., 2005) although it may be less evident for untrained subjects (Chholak et al., 2019). Thus, MI-based BMIs offer multiple advantages: from the use of endogenous signals to the possibility to target specific limbs due to spatial characterization of these patterns. Importantly, such BMIs can be also operated in a self-paced way (i.e. subjects can voluntarily activate it) since independent of any system. Because of this, MI-based BMIs patterns have been extensively studied, in rehabilitation where the principle is to stimulate the damaged limb, facilitating neuroplasticity via proprioceptive feedback.

Most MI-based BMIs are based on sustained MI and usually compare activities between two states such as hand MI (imagining hand movement) versus a resting state (Biasiucci et al., 2018; Perdikis et al., 2018). This approach allows BMI users to trigger predefined commands once the appearance of patterns specific to the active state is detected. The user is usually

confronted to paradigms where they are instructed to continuously perform either one (e.g. hand MI) or the other state (e.g. resting state, REST) continuously during a certain amount of time (see Fig. 1.2). The feedback is delivered visually, for example thanks to a bar representing the likelihood of the user to be in one of the states. The decision is given only once the bar reaches one of the arrows.



Figure 1.2 – Common scenario for MI-based BMI. A user is put in front of a screen showing visual feedback. The grey bar is moving towards one of the two arrows and represents the likelihood of the user to perform the MI action. The decision is taken when the bar reaches one of the arrows.

1.4 Movement termination in BMI

So far, we have considered MI as a sustained action. However, MI can be also defined in terms of motor state transitions such as a movement execution (ME) where an initiation (onset) and a termination (offset) can be monitored. In such a scenario, the initiation of a movement such as a hand action (ME or MI) will be characterized by an ERD in both μ and β bands while the termination of hand movement (MI termination, MIt) will elicit an ERS in the β band.

1.4.1 Neural correlates of movement termination

During movement termination, an increase of power can be observed and is known as the β rebound. Such a phenomenon can last for a second and was well observed in the case of MI (Pfurtscheller et al., 2005) or in response to somatosensory stimulation (Neuper and Pfurtscheller, 2001). During hand MI, β rebound is mainly observed in the contralateral hand representation of the sensorimotor cortex. Additionally, it is also often reported in the supplementary motor area (SMA) located in mid-central areas with slightly higher frequencies as well as an earlier beginning compared to contralateral ERS. This might be explained by the involvement of at least two neural networks in a cross-talk (Pfurtscheller, Woertz, et al., 2003; Pfurtscheller, Neuper, Pichler-Zalaudek, et al., 2000). Although the role of β rebound is still under debate, different hypotheses have been suggested for the role of beta oscillations. Notably, the β rebound is thought to have an inhibitory role by reflecting a mechanism of functional inhibition of the motor cortex by somatosensory processing (Cassim et al., 2001; Houdayer et al., 2006). The correlation found between β amplitude and the concentration of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) (Gaetz et al., 2011) can be

seen as a strong argument for this hypothesis. Regarding its functional role, the "status quo" hypothesis supports that β oscillations reflect an active process promoting the existing motor set to maintain the current sensorimotor or cognitive state (i.e. status quo) (Engel and Fries, 2010).

1.4.2 Beta-rebound based BMIs

Mostly referred to as β rebound-based BMI (Bai et al., 2007; Jeon et al., 2011; Pfurtscheller and Solis-Escalante, 2009), the use of this signal could lead to new BMIs where the subjects would not need extensive training since the difference of band power amplitude between ERD and ERS is much stronger than the one between ERD and the resting state (Stancák Jr and Pfurtscheller, 1996). Hence, this difference could yield to higher performances.

Based on this hypothesis, few studies have explored the feasibility of decoding motor termination. In 2007, Bai et al. investigated the detection motor termination through their system based on β rhythm and showed the potential use that such an approach could have (Bai et al., 2007). The system was tested on a binary cursor-control game where users reached high performances without extensive training. Importantly, this study was also tested successfully on two patients (one patient with amyotrophic lateral sclerosis, one stroke patient). Again, β rebound was found during hand MI and ME tasks in healthy subjects as well as in both of these patients. Hence, the presence of β rebound in these patients, as well as the short training could be an ideal candidate for clinical applications. Additionally, Pfurtscheller introduced in 2009 the concept of brain switch with a system based on only one EEG channel (Pfurtscheller and Solis-Escalante, 2009). Here, their approach was based on the detection of post-movement β rebound induced after foot MI allowing users to activate or deactivate a BMI. The channel was set on the vertex where the β rebound was found most stable and similar to the actual movement (G. R. Müller-Putz et al., 2007). The use of the brain switch was later extended with real foot movement for decoding calibration and direct use during MI task in healthy subjects (G. R. Müller-Putz et al., 2010). The combination with other brain signals such as SSVEP was also investigated to control an orthosis (Pfurtscheller, Solis-Escalante, et al., 2010). However, this control was primarily based on an incongruent MI (i.e. subjects were asked to activate a hand orthosis using movement imagination of their feet). Hence it would be interesting to investigate how a congruent MI could be used to stop the control of an orthosis. To the best of our knowledge, there is no study clearly showing the benefit of using β -rebound BMIs when comparing with a more classical approach (MI vs resting state). Such analyses would be then primordial to fully understand how such BMIs can be used.

1.5 BMIs and physiological signals

As we saw, SMR-based BMIs are characterized by ERD/S patterns. In these BMIs, only signals originating from the central nervous system are usually considered while other biosignals -such as respiratory or cardiac signals- are treated as physiological noise (Pfurtscheller, Ortner,

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et al., 2010). Despite such assumptions, a growing literature is reporting that physiological signals such as skin conductance, heart rate, skin temperature or respiration rate could provide additional information regarding the motor intent of a user. Accordingly, the broader concept of Body-Machine Interfaces recently emerged in the field. In contrast to BMIs, Body-Machine Interfaces exploit signals originating from the peripheral autonomic nervous system (ANS) and present the great advantage to be monitored easily while requiring only a minimal time to set-up. The use of physiological signals alone has been shown to contain enough information to detect movement execution (Marchal-Crespo et al., 2012) with high reliability. Even more, hybrid Brain-Machine Interfaces have also shown that the combination of EEG signals with such physiological signals could boost the currents BMIs for example in the case of music imagery (Falk et al., 2010), motor imagery (Pfurtscheller, Allison, et al., 2010; Shahid et al., 2011) or movement execution (Zimmermann et al., 2013).

Although the use of physiological signals in these novel BMIs has been adopted by the community, physiological effects on BMIs are still largely unknown while being covered in many other fields. Notably, breathing has been found to have a key effect on numerous human functions, including, perceptual (Perl et al., 2019) and cognitive functions (Nakamura et al., 2018; Zelano et al., 2016). This effect was was also reported on motor functions (Bramble and Carrier, 1983; Park et al., 2020). Indeed, breathing was recently shown to be coupled with higher-level motor control functions such as voluntary action (Park et al., 2020). In this last study the authors reported that the initiation of a voluntary action tends to be in the expiration phase. Moreover, the authors also showed that respiratory phases modulate the RP (first component of MRCP) as well suggesting that fluctuations of brain activity are driven by the breathing signals. These findings could be particularly relevant in the BMI field. Indeed, as explained previously, BMIs aim to have a natural interaction by exploiting endogenous signals such as MRCPS or SMRs with both signals observed during movement execution but also during MI task. Hence, following such findings, one interesting question would be to investigate how breathing impacts BMIs and particularly those based on MI paradigm.

1.6 Thesis outline

In this work, I will consider the motor state transitions associated with the MI task for EEGbased BMI. Here, I will put a particular emphasis on the termination of upper limb movements and investigate the use of such an approach aiming to decode the stopping process occurring after movement imagination. To do this, I will pursue a three-fold objective:

- Characterization of the motor termination transition
- Evaluation and validation of the decoding approach in closed-loop scenarios
- Module integration and interaction with BMIs components

The first step will be the characterization of the process occurring in motor termination.

This step will aim to understand which neural correlates are exhibited in such a process. Using such correlates, our second step will be to develop an approach for detecting motor termination. First of all, this approach should be validated based on the current BMIs metrics and its benefits should be demonstrated and compared to the state-of-the-art approaches. Since the assessment of closed-loop interactions on the system performance is critical within this field, an online evaluation should also be performed. Finally, the integration of such a module with existing BMIs should also be correctly investigated. In this third and last step, we will understand how both motor transitions could be decoded in the same BMIs. More, the interaction with other component such as BMI effectors should be carefully studied since they play an important role in rehabilitation therapy and are used to promote movement (Biasiucci et al., 2018) and facilitate neuroplasticity mechanism (Zieliński, 2006) (i.e. ability of neurons to change through growth and reorganization). Hence, investigate how these effectors are affecting the neural correlates of motor termination as well as our decoding approach is primordial.

To characterize those motor state transitions, although neural correlates are indeed the primary source of information for the design of BMIs, I also briefly introduced that other physiological signals could also contain valuable information for BMIs. Hence, in a second part of this thesis, I will also raise the question about the role of the interoceptive system during those motor state transitions. Particularly, my goal will be to understand how physiological signals such as breathing signals can affect the BMIs and how monitoring breathing signals could enhance BMI performances.

The structure and the next chapters of this thesis can be summarized as follows:

In **Chapter 2 (User adaptation to closed-loop decoding of motor imagery termination**), I study how the decoding of motor termination can be performed during MI tasks. I investigate how a user could learn to adapt to such a decoder in the framework of a closed-loop BMI in order to control its interruption. Results show that detecting MI termination has an intrinsic latency mainly due to the late appearance of neural correlates of motor termination; however, and critically, this latency can be compensated by BMI users. This compensation is only possible because of the reliability of the decoder as well as the consistency of offset correlates, which makes it possible for users to predict their BMI dynamics.

In **Chapter 3** (Stopping versus resting state during motor imagery paradigm), I investigate the difference between motor termination and resting state based on neuroimaging and decoding aspects. I also study how the discussed approach would benefit BMI users and provide some insight on the combination with classical SMR-based BMIs. Results show that decoding MI termination based on the correlates of motor termination is not only more reliable but also allows a faster detection. Two different alternatives are also described for combining with standard SMR-based BMIs which consist in (1) either the use of finite state machine combining decoding for the onset (rest-to-movement transition) and the offset (movement-to-rest transition) of MI or (2) to use a three-class model trained to distinguish the

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three different periods, i.e. resting state, MI and MI termination.

In **Chapter 4** (Effects of exoskeleton on correlates of motor termination for Brain-Machine Interface), I focus on the impact of BMI effectors on the correlates of motor termination. The use of BMI effectors such as orthosis is often linked to the BMI system to trigger specific movements. To be able to stop an action, the user must be able to produce the correlates of motor termination while enduring a passive movement. Hence, in this part, I study the impact of such effectors on these correlates and compare the decoding accuracies with respect to a pure MI task. I show that β rebound can occur during passive movement while wearing an exoskeleton hand-induced motion. More, I show that this rebound is similar to the one observed during the pure MI task although more localized in central and ipsilateral channels. The presence of such markers promotes reliable decoding of motor termination under passive movement.

In **Chapter 5 (Breathing affects MI-based Brain-Machine Interfaces)**, I investigate how breathing affects SMR-based BMIs. In particular, I evaluate how the breathing process affects the correlates of MI (ERD in μ and β bands) as well as the BMI performance. The results provide an extensive analysis regarding the effect of the breathing cycle specifically on μ -ERDs, showing stronger ERD during the late expiration phase. Moreover, I identify a link between breathing and performance and propose that breathing signals are a valuable predictor for BMI performance. This highlights the importance of monitoring such signals and places the respiratory system as a key component of motor preparation and motor imagery.

Finally, in **Chapter 6** (General Discussion), I present a summary of the results of this thesis and provide a general discussion on how it contributes to the field and the future work that could be done on the top of these findings.

1.7 Personal Contributions

Study 1: B. Orset, K. Lee, R. Chavarriaga, J.d.R. Millán, User adaptation to closed-loop decoding of motor imagery termination (Published in IEEE Transactions on Biomedical Engineering) Personal Contribution: Experimental design, recording, analysis, writing

Study 2: B. Orset, K. Lee, R. Chavarriaga, J.d.R. Millán, Stopping versus resting state during motor imagery paradigm (In Preparation) Personal Contribution: Experimental design, recording, analysis, writing

Study 3: B. Orset, K. Lee, R. Chavarriaga, J.d.R. Millán, Effects of exoskeleton on correlates of motor termination for Brain-Machine Interface (In Preparation) Personal Contribution: Experimental design, recording, analysis, writing

Study 4: B. Orset, S. Betka, O. Blanke, Breathing affects MI-based Brain-Machine Interfaces (In Preparation)

Personal Contribution: Experimental design, recording, analysis, writing

Chapter 1

B. Orset, K.Lee, R. Chavarriaga, J.d.R. Millán, Reliable decoding of motor state transition during an imagined movement (Published in 2019 9th International IEEE/EMBS Conference on Neural Engineering, Conference Paper)

Personal Contribution: Experimental design, recording, analysis, writing

I. Iturrate, S. Martin, R. Chavarriaga, **B. Orset**, R. Leeb, A. Sobolewski, E. Pralong, M. Castro-Jiménez, D. Benninger, J. Bloch, J.d. R Millán, Beta-driven closed-loop deep brain stimulation can compromise human motor behavior in Parkinson's Disease (Published in BioRxiv) Personal Contribution: Analysis, writing

L. Tonin, T. Kuzu, J. Pardo, S. Perdikis, **B. Orset**, K. Lee, M. Aach, T. A. Schildhauer, R. Martínez-Olivera, J. del R. Millán, A brain-controlled wheelchair for people with severe tetraplegia after spinal cord injury (Submitted)

Personal Contribution: Experimental design, recording

G. Dominijanni, **B. Orset**, C. Pierella, S. Shokur, S. Micera, A Modular Platform For The Assessment of Extra Limbs Sensorimotor Control Strategies (Submitted, Conference Paper) Personal Contribution: Experimental design, Conception, recording, review

2 User adaptation to closed-loop decoding of motor imagery termination

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Abstract

One of the most popular methods in non-invasive brain machine interfaces (BMI) relies on the decoding of sensorimotor rhythms associated to sustained motor imagery. Although motor imagery has been intensively studied, its termination is mostly neglected. Objective: Here, we provide insights in the decoding of motor imagery termination and investigate the use of such decoder in closed-loop BMI. *Methods:* Participants (N = 9) were asked to perform kinesthetic motor imagery of both hands simultaneously cued with a clock indicating the initiation and termination of the action. Using electroencephalogram (EEG) signals, we built a decoder to detect the transition between event-related desynchronization and event-related synchronization. Features for this decoder were correlates of motor termination in the upper μ and β bands. *Results*: The decoder reached an accuracy of 76.2% (N = 9), revealing the high robustness of our approach. More importantly, this paper shows that the decoding of motor termination has an intrinsic latency mainly due to the delayed appearance of its correlates. Because the latency was consistent and thus predictable, users were able to compensate it after training. Conclusion: Using our decoding system, BMI users were able to adapt their behavior and modulate their sensorimotor rhythm to stop the device (clock) accurately on time. Significance: These results show the importance of closed-loop evaluations of BMI decoders and open new possibilities for BMI control using decoding of movement termination.

2.1 Introduction

Brain machine interfaces (BMIs) aim at providing communication and control pathways for people with motor disabilities (Millán et al., 2010). A BMI bypasses the natural motor pathways enabling users to control a large variety of external devices and interact directly with their environment, as the BMI decodes users' intentions directly from the analysis of brain signals and translates intentions into commands for an external device such as spellers (Birbaumer et al., 1999; Perdikis et al., 2014), avatars (Perdikis et al., 2018), robots and wheelchairs (Galán et al., 2008; Leeb et al., 2015) , hand neuroprostheses (G. R. Müller-Putz, Scherer, Pfurtscheller, et al., 2005; Tavella et al., 2010) as well as for neurogaming and consciousness assessment (Beveridge et al., 2019; Coyle et al., 2015).

Most non-invasive BMIs based on voluntary modulations of brain rhythms aim at detecting the initiation of an imagined movement. Hence decoders are usually trained on samples from the periods before and after onset. Once the onset is detected, predefined commands can be triggered. Although the detection of imagined movement initiation is critical in the process, decoding the volitional interruption of motor imagery (MI) is of equal importance in order to endow brain-actuated devices with more natural behavior. While decoding of movement initiation is the focus of multiple works (Lew et al., 2012; G. R. Müller-Putz, Scherer, Pfurtscheller, et al., 2005; Niazi et al., 2011; Tavella et al., 2010), decoding of movement termination has been rarely investigated (Rae et al., 2014; Schultze-Kraft et al., 2016). Indeed, only two studies have explored so far, the feasibility of decoding termination of MI. The first one showed the possibility to build a brain switch using one Laplacian channel ((Pfurtscheller and Solis-Escalante, 2009). Similarly, Bai et al. ((Bai et al., 2007) investigated a β rhythm-based BMI in repetitive motor imagery.

In this study, we investigate the use of a specific decoder for hand MI termination in a closedloop BMI. We show for the first time that, during closed-loop operation, BMI users can adapt to their own decoder and compensate for its latency to stop precisely on time. To this end, we designed a task enabling us to capture the correlates of sustained MI as well as the neural correlates of MI termination. This task was inspired by Libet's experiment on motor initiation (Libet et al., 1993) and explored in the context of BCI (Pereira et al., 2018). It is known that changes in the brain rhythms during planning and execution of movements, as well as in the case of MI, can be observed in and decoded from human EEG (Pfurtscheller et al., 2006). After movement termination, an increase of power (event-related synchronization, ERS) is induced in the β band (13–25 Hz). Such synchronization, often called β rebound, can last for about a second. Although the role of β rebound is still under debate, it is currently thought to have a function of inhibition of the motor cortex by somatosensory processing (Cassim et al., 2001; Houdayer et al., 2006). Oscillatory activity in the β band has been also linked to an active process aiming to maintain the current sensorimotor or cognitive state (i.e., status quo) (Engel and Fries, 2010). Similarly, it has also been reported the presence of an ERS in the μ band (8-13 Hz) that could be interpreted as an electrophysiological correlate of cortical idling state in sensorimotor areas (Pfurtscheller, 1992; Pfurtscheller and Neuper, 1994; Pfurtscheller et al., 1996). Such synchronizations can be explained by an increase of rhythmic activity paradoxically due to a decrease of excitability of cortical neurons or inhibited cortical neurons (Pfurtscheller, 2001; Pfurtscheller and Lopes Da Silva, 1999). This was also reported after MI tasks (Pfurtscheller, 2001). When performing hand-related motor tasks, ERS can mainly be observed in the contralateral hand representation area. In the β band, this synchronization can also be seen in the supplementary motor area (SMA) located in mid-central areas of the brain with slightly higher frequencies and an earlier beginning compared to the contralateral ERS (Pfurtscheller, Woertz, et al., 2003; Pfurtscheller, Neuper, Pichler-Zalaudek, et al., 2000).

2.2 Methods

2.2.1 Experimental setup

Nine healthy naïve subjects (19–26 years, 2 females) participated in the experiment. The study was approved by the Cantonal Committee of Vaud, Switzerland for ethics in human research (CER-VD) and subjects gave their written permission and signed a consent form.

2.2.2 Offline Protocol

Participants were comfortably seated in front of a PC monitor and asked to perform kinesthetic MI (i.e., imagining the feeling associated with performing a movement) of both hands

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simultaneously. The total duration of a trial was 13 s. Subjects first fixated the cross in the middle of the screen (3 s), then they were instructed to performed MI once the clock hand was moving (2 to 4 s), and finally were asked to stop their MI and stay calm until the hand clock finishes its turn (6 to 8 s). The total time of a clock hand revolution (MI plus rest) was 10 s. During the rest period after MI termination (MIt), subjects were instructed to stay calm avoiding any muscular contraction or blinks while the hand finished to revolve around the clock. In between trials, a relaxation phase of 7 s was introduced to allow participants to blink and rest. Fig. 2.1 illustrates the structure of the trial. Each subject performed 4 runs of 30 trials each (120 trials in total).



Figure 2.1 – Trial structure during offline protocol. During a trial, the subject is asked to continuously look at a fixation cross in the center of the clock. The subject is instructed to stay calm for the first 3 seconds without moving or blinking. A clock hand (green bar) indicates to the subject to initiate his motor imagery of both hands. When the clock hand reaches a target (red bar), the subject stops motor imagery and stays at rest (no blink or movement). A period of 7 seconds following each trial allows the subject to relax.

2.2.3 Online Protocol

After training a decoder on the offline data (c.f. Section 2.2.6), participants' task was to stop the clock hand on a target in real-time by terminating their MI action. Participants were asked to adapt to their individual decoder in order to stop precisely on the target. To do so, participants had to evaluate the latency of the BMI output during an initial calibration phase that preceded the actual experiment. The calibration phase consisted of 20 online trials and, afterwards, each subject performed 4 runs of 25 trials each (100 trials in total). In this protocol, a gauge (not shown in Fig. 2.1) was additionally integrated on the clock hand showing the BMI output as a source of continuous feedback. The clock hand stopped when the gauge was filled ($P_{gauge,t} = 1$). The BMI output corresponded to the integration of the output probabilities of the MIt decoder to each single EEG sample based on an exponential moving average (Eq. 3.1) (Perdikis

et al., 2011):

$$P(t) = \alpha P(t) + (1 - \alpha) p(t)$$
(2.1)

Where P(t) is the smoothed likelihood, p(t) is the likelihood of detecting MI termination (output of the MIt decoder) and α is a smoothing parameter, $0 \le \alpha \le 1$. The smoothing parameter α was individually set for each subject by the operator during the calibration phase. The value of α was manually tuned so as to optimize correct delivery, increasing it in the case of substantial early delivery over the last few trials or decreasing it in the case of long late delivery. At the end of the calibration phase, the value of the smoothing parameter α was kept fixed for the entire online evaluation. Table 2.1 reports the value of this parameter for each subject. To decrease the delay due to the exponential moving average, the smoothed probabilities were passed through a burst framework which was gradually increasing the bar shown to the user. This burst framework was defined by the following equation (Eq. 2.2).

$$\begin{split} P_{gauge}(t) &= P_{gauge}(t-1) + (P(t)-0.5) \\ P_{gauge}(t) &\leq 1 \\ P_{gauge}(t=0) &= 0.1 \end{split} \tag{2.2}$$

Table 2.1 – Individual values of the smoothing parameter α used during the online session. The posterior probabilities of the decoder were smoothed using exponential moving average based on equation 1 with α parameter set for every subject during a calibration phase of 20 trials.

Subject	s01	s02	s03	s04	s05	s06	s07	s08	s09
α	0.9	0.75	0.8	0.65	0.8	0.65	0.7	0.8	0.8

2.2.4 Recording system

EEG signals were recorded at a sampling frequency of 512Hz with 16 active surface electrodes placed over the sensorimotor cortex i.e., on positions Fz, FC3, FC1, FCz, FC2, FC4, C3, C1,Cz, C2, C4, CP3, CP1, CPz, CP2, and CP4 according to the international 10/10 system (reference: left earlobe; ground: AFz; gtec gUSBamp, Guger Technologies OG, Graz, Austria). The amplifier was set with a hardware band-pass frequency between 0.01 and 100 Hz (Butterworth 4th order) and a notch filter between 48 Hz and 52 Hz. A common average reference was used on the EEG raw data to enhance the signal-to-noise ratio.

2.2.5 Offline Classification

Power spectral densities (PSD) were computed in a 1s-window using the Welch's method (0.5 s window with 0.25s non-overlapping window) from 4 to 40 Hz with a 2 Hz resolution on the 16 channels, yielding a total of 304 features. We compared three different classifiers based on different bands: μ band (8–13 Hz), β band (20–26 Hz) and all bands together (4–40 Hz). Then for each of these classifiers, 10-fold trial-based cross-validation was performed where the 6 best features from each fold were selected based on their Fisher Score. Using these features, a Diagonal Linear Discriminant Analysis (DLDA) was trained. Feature vectors were extracted from each sample in the training dataset and z-score normalized. Their mean and variance were applied on the feature vectors in the testing dataset. The movement termination decoders were trained to distinguish between sustained MI and MIt. 1-second-long samples were computed with a sliding window (shifted every 62.5 ms) in the time intervals [-2, 0] s (MI) and [0.5, 2.5] s (MIt) with respect to the offset (t=0). Using the 1s-long overlapping sliding windows every 62.5 ms within the 2 s interval yield 17 samples per trial. To assess the classification performance, we calculated the accuracy at the sample level over the 10-fold cross validation. The accuracy was defined as the number of correctly classified samples over the total number of samples and was computed for each fold. We estimated the significance threshold above chance level at the 95% confidence interval based on the inverse binomial cumulative distribution (uniform priors, n=408 samples in test set), leading to a value of 54.17%.

2.2.6 Asynchronous Classification in online session

Based on the results of the cross-validation, and using all the data from the offline session, we trained a decoder using all the 304 features available (4–40 Hz). After normalization, a total of 6 features were selected based on their Fisher Score ranking. Then, these features were used to train a DLDA classifier to detect MIt in real-time during the online session. During this session, a 1s buffer was used and updated every 62.5 ms. For each buffer, PSDs were z-scored using the mean and the standard deviation found when training the decoder.

2.2.7 Pseudo-online analysis

A pseudo-online (PO) analysis was performed on the offline and online data to further study the classifier behavior in real-time at the trial level. To do so, we compare the behavior of the online classifier (online PO) and the behavior of the different classifiers used for cross-validation (offline PO). In this analysis, the classifier was tested in the time interval [-3, 4] s with respect to the offset cue. During this time interval, the likelihood (i.e., the probability of detecting MIt) was calculated from the decoder on samples computed with a 1s-window shifted every 62.5 ms. The posterior probabilities were then smoothed as explained in Section 2.2.3. Using this decoder, we measured the decoding latency, which we defined as the time when the average posterior probabilities over trials were crossing the significance threshold

above chance level of 54.17%.

2.3 Results

2.3.1 Time frequency Analysis

A spectral analysis was first performed on central channels (C3, Cz, C4) in order to evaluate the event-related spectral changes for MI onset and offset using a Fast Fourier Transform on 1s-Hanning window shifted every 62.5 ms (Makeig, 1993). A baseline period [-2, -1] s with respect to the onset was used to compute the spectral changes. Fig. 2.2A shows the grand averages across subjects recorded during the offline session. During sustained MI, a desynchronization (ERD) could be observed in the μ and β bands, more prominently on centrolateral channels (C3, C4) as expected in the case of bilateral hand MI. On the opposite, an ERS was seen on these channels after stopping MI, mainly noticed in the upper μ (11–13 Hz). An ERS was also observed in the high β band (20–30 Hz) mainly in C3 and C4, but it exhibited larger inter-subject variability. Importantly, one can observe that β ERS had a shorter duration than μ ERS (Fig. 2.2B). Indeed, β ERS started at about 0.8 s after the offset and lasted for 2.1 s, while μ ERS started later at 1.5 s but remained until the end of the trial (α =0.05, repeated measure t-tests based on t-statistics, FDR corrected for multiple comparisons).


Figure 2.2 – **A.** Grand average spectrogram on central channels across subjects and averaged over all trials during offline session. The first vertical line corresponds to MI onset (ON), while the second one is MI offset (OFF). The figure has been interpolated due to the variation on MI duration. The pre and during MI period [-3, 4] s was cropped and joined with the post MI period [0, 6] s. ERD/ERS were computed with a logarithmic scale using a baseline period [-2, -1] s. **B.** Bandpower of the μ and β rhythms averaged over C3 and C4 channels for all the trials. The time origin (t = 0) corresponds to the offset. Each color bar on top indicates periods of significant difference with respect to the baseline period ([-3, -2] s from MI onset) for its respective band (α = 0.05, repeated measure t-tests based on t-statistics, FDR corrected for multiple comparisons). **C.** Time intervals used for classification: [-2, 0]s (MI, class 0) and [0.5, 2.5] s (MI termination, class 1) with respect to the offset (t = 0).

2.3.2 Offline Classification

We evaluated the performance of our classifier for decoding MI termination with three different bands: μ (8–13 Hz), β (20–26 Hz) and all bands (4–40 Hz). Fig. 2.3A shows the accuracy of the three decoders for each subject and in grand average. The μ and β bands-based decoders

yielded accuracies of 73.3 ± 7.4 % and 73.0 ± 7.0 % (mean ± std), respectively, while using all bands reached an accuracy of 76.2 ± 6.4 %. This performance improvement using the classifier based on all the bands was, however, not statistically significant on average (one-way ANOVA, F(2, 24) = 0.57; p = 0.574). Importantly, all three classifiers reached high accuracy and were statistically above the significance threshold (54.17%) for every subject. Additionally, Fig. 2.3B shows the Fisher scores of the spectral features averaged over the different folds of the cross validation and subjects in the case of the third classifier. Note that most of the discriminant features can be found in channels located over the hand motor area (C4, C3 and CP4) in the upper μ band and, to a lesser extent, in the β band. Later, we used this classifier for the online session.



Figure 2.3 – Movement termination decoder. **A**. Classifier accuracies are reported for every subject (s1-s9) as well as in grand average (GA). The standard deviation is shown on each bar. Dots indicate performance for each subject. The horizontal dashed line corresponds to the significance threshold above chance level (54.17%). **B**. Fisher score map averaged over all subjects. Fisher scores are shown for the features (channels x frequencies). Higher values (i.e., yellow color) indicate highly informative features while blue colors indicate less discriminant features. The scores were normalized for each subject using min-max scaling.

2.3.3 Asynchronous Classification

For online session, we trained, for each subject, a decoder such as described in Section 2.2.7. Fig. 2.4 reports the features that were selected for the online decoders. Most of the features were located in the upper μ band. Fig. 2.5A shows the latency for each subject during the online session when using our integrative framework for increasing the reliability of BMI outputs (see Section 2.2.3). The latency was computed for every trial by calculating the difference between the time when the participant is supposed to stop and when the clock hand actually stopped moving. On average, we obtained a latency of 0.1 s ± 1.7 s (median ± diff. percentile). Fig. 2.5B reports the number of trials where MI termination was detected on average, in 85.44% of the trials. For the remaining trials, the clock hand continued rotating for 10 s until the end of the trial. Interestingly, Fig. 2.5B illustrates that subjects with a high accuracy (≥ 80%) also exhibited a small median latency. These results show that participants were able to control the offset of their MI precisely. More importantly, these results indicate that the latency is consistent over the trials because of a relatively small inter-trial variability in most of the subjects (except subject s8).



Figure 2.4 – Feature occurrences for online decoding for all subjects. The number of times a feature was selected for online classifier was counted across subjects. Higher values (i.e., yellow color) indicate highly selected features while blue colors indicate less selected features



Figure 2.5 – Latency distribution during closed-loop scenarios. **A**. Distribution of latency for every trial and for each subject. Each point corresponds to the latency of one trial and was calculated by computing the difference between the time when the participant is supposed to stop and when the clock hand stopped to move. Boxplots illustrate the distribution and the median latency for every subject. **B**. The graph shows the median latency in function of the percentage of trials where a stop was detected for each subject.

2.3.4 Pseudo-online Classification

We further investigated the behavior of our approach, comparing its dynamics between offline and online sessions. To do so, we performed a pseudo-online analysis of the offline session (offline PO), the calibration phase, and each run of the online session (online PO). The results are reported in Fig. 2.6. On average across all subjects, one can observe that the online PO is shifted back in time, crossing the 54.17% significance threshold above chance level at $t = 0 \pm$ 0.11 s (mean ± SEM) before offset cue, while the offline PO crosses it at $t = 1.25 \pm 0.15$ s (mean ± SEM) after the offset cue as expected. The calibration phase exhibits a similar behavior to the offline PO. Additionally, we can see that the latency was consistent over online runs. These results confirm that subjects learned rapidly to adapt to the latency of their decoder during closed-loop BMI usage and were able to stop the clock hand precisely on time.



Figure 2.6 – Comparison of pseudo-online analysis between offline and online sessions. The figure shows the grand average of decoding likelihood over all subjects in a time interval [3, 4] s with respect to the offset as well as the respective standard error on each time point. The horizontal red line corresponds to the significance threshold above chance level of 54.17%. The filled black line corresponds to the pseudo-online analysis performed on the offline session, while the blue one corresponds to the online session. The dash lines show each individual runs of the online session as well as the calibration phase. The vertical dash lines show where the each pseudo-online is crossing the significance threshold for the offline session and the online session (average over all 4 runs).

2.3.5 ERS modulation during online session

We computed the spectrogram in central channels during the online session (Fig. 2.7). Compared to the offline session (Fig. 2.2A), one can observe a temporal shift of both ERS in the upper μ and β bands that appear now aligned to the offset cue (Fig. 2.7A). Interestingly, we can also notice stronger ERS patterns, especially in the β band. This may be explained by subjects who have more MI practice. Similarly, we evaluated the timing of μ and β ERS (α =0.05, repeated measure t-tests based on t-statistics FDR corrected for multiple comparisons). As Fig. 2.7B illustrates, during the online session, the β ERS appeared at t = -1.1s; while, as before, the μ ERS started to develop slightly later at t = -0.8s with respect to the offset cue. Interestingly, ERS in both bands seemed to last until the end of the trials, as shown by the significant differences w.r.t. the baseline period (top-colored bars in Fig. 2.7B). Additionally, we also computed the spectrogram for channels C3 and C4 at the single trial level (Fig. 2.8) from every subject in order to investigate the inter-trial variability across the different bands that cannot be observed in the grand average spectrogram. One can notice that the upper μ ERS is well aligned with the offset cue and is consistent over trials. On the other hand, there is a large variability of the β rebound over the trials and, more importantly, it is less well aligned with the offset cue.



Figure 2.7 – Time-Frequency Analysis on central channels during closed-loop paradigm. **A**. Grand average spectrogram on central channels across subjects and averaged over all trials during the online session. The first vertical line corresponds to the onset (ON) when users initiate their MI, while the second one is the offset (OFF) and corresponds to the time when they stopped MI. The figure was interpolated due to the variation on MI duration. The pre and during MI period [-3, 4] s was cropped and joined with the post MI period [0, 6] s. ERD/ERS were computed with a logarithmic scale using a baseline period [-2, -1] s. **B**. Band-power of μ and β band averaged over C3 and C4 channels for all the trials. The time origin corresponds to the offset. Each color bar on top indicates periods of significant difference with respect to the baseline period ([-3, -2] s with respect to the onset) for its corresponding band (α =0.05, repeated measure t-tests based on t-statistics, FDR corrected for multiple comparisons).



Figure 2.8 – Average band power of μ and β bands over trials collected from all subjects during the online session. All trials including every subject are represented on these heat maps ordered by increasing offset cue time. The first line (black) corresponds to the onset cue where the participant initiates his motor imagery, while the second one (blue) is the offset cue and corresponds to the time when the participant should stop the clock hand. The top panel illustrates, the μ band, while the bottom panel corresponds to the β band

2.4 Discussion

The present study investigated the feasibility of decoding the spontaneous termination of an imagined movement, based on the natural electrophysiological correlates of such a task. More importantly, we also aimed to answer whether BMI users were able to control the offset of their sensorimotor rhythm in real-time to stop a device accurately at a specific position. We evaluated such an ability by analyzing the BMI performance accuracy and latency.

2.4.1 Time-frequency analysis

From our time-frequency analysis, we observed neural correlates of motor termination consistent with literature (Pfurtscheller, 2001; Pfurtscheller and Lopes Da Silva, 1999; Pfurtscheller et al., 2006). These correlates are characterized by an increase of power in the upper μ and β bands. Comparing these correlates, it appears that the μ ERS is more prominent and more reliable over subjects since it was observed in eight of them, while significant β ERS was found in five subjects. A similar observation has been done in (Pfurtscheller and Solis-Escalante, 2009) where, after stopping foot MI, μ ERS was also reported for some subjects. Moreover, this μ ERS tends to last longer than β ERS, which likely help in detecting MI termination. This

difference of duration can be explained by their functional role. Indeed, β rebound is identified as a neural correlate of termination (Cassim et al., 2001; Engel and Fries, 2010; Houdayer et al., 2006), while μ rebound is reported as a neural correlate of an idling process (Pfurtscheller, 1992; Pfurtscheller and Neuper, 1994; Pfurtscheller et al., 1996). Because of these different roles, β rebound can be seen more as a phasic modulation at offset, whereas μ synchronization is expected to remain as it is the paradigmatical pattern at rest. Thus, our results are consistent with the current hypotheses regarding the functional roles of both β and μ rhythms (Cassim et al., 2001; Engel and Fries, 2010; Houdayer et al., 2006; Pfurtscheller, 1992; Pfurtscheller et al., 2006; Pfurtscheller and Neuper, 1994; Pfurtscheller et al., 1996). Importantly, these correlates are found mainly over the sensorimotor cortex (C3 and C4) as well as for some subject in central channel Cz. The location of these correlates is consistent also with fMRI literature for movement termination (Coxon et al., 2012; Rae et al., 2014; Swick et al., 2011). Indeed, premotor supplementary area (preSMA) and premotor cortex were identified as brain region involved in the process of stopping a voluntary action. It is also known than the β rebound is mainly observed in premotor cortex as well as supplementary motor area (Pfurtscheller, Woertz, et al., 2003; Pfurtscheller, Neuper, Pichler-Zalaudek, et al., 2000). Hence, these results support the putative role of these correlates in the termination of a motor action.

2.4.2 Decoding motor imagery termination

Performance of our decoder were similar to those reported by Bai et al. (Bai et al., 2007) (average accuracy of ~76% and ~75%, respectively). Nevertheless, and importantly, during closed-loop operation, performance of our decoders increased to ~85% with a negligible latency (see next section for further discussion). Although our decoder followed the same strategy, the studies mentioned above focused on the β band. In contrast, we found that additional information can be extracted from the upper μ band (see Figs. 2.3B and 2.4). Furthermore, the comparison between decoders based on different frequency bands did not show significant differences in term of accuracies. These observations indicate that BMIs should not be based on preselected physiological features that may vary from subject to subject, but should be personalized accordingly –e.g., using feature selection on a broader frequency range as done in the present work.

2.4.3 Decoding latency and adaptation

By looking at the offline PO analysis, we can observe that our decoder shows an average latency close to 1.4 s. This latency can be explained mostly by the neurophysiology of ERS. Indeed, ERS develops around 1 s after MI offset, which makes an earlier detection implausible. In contrast, the online evaluation (online PO) exhibits decreased average latency with values close to the MI termination cue. We can thus conclude that, based on the BMI feedback provided by the decoder, subjects were able to adapt and compensate the decoding latency, likely by anticipating the right moment to stop MI. By looking at the spectrograms in the grand average and at the trial level (Figs. 2.2, 2.7, and 2.8), it appears that the neural correlates of

Chapter 2 User adaptation to closed-loop decoding of motor imagery termination

MI termination in the upper μ band are much more consistent between subjects and show a higher inter-trial stability than in the β band. This consistency leads to a robust decoding of motor termination and make the responses of the system more predictable. This probably enabled users to stop accurately on target. On the other hand, β modulations seem also to play a critical role during the closed-loop experiments, supporting that the decoders are detecting MI termination and not just the rest state after the end of the task. Although in the offline condition the performance curve of the detector shows a plateau (Fig. 2.6), indicating that there might be a strong component of rest, this is not the case once subjects go online and learn to anticipate (and eventually modulate) their brain signals. The sharper detection curve for the online sessions (Fig. 2.6), decaying about 1 s after t = 0, suggests that the classifier is not simply decoding the rest state, but a fast transitory EEG correlate associated to MI termination. This correlate is likely the β rebound observed in Fig. 2.7, which is initially very prominent and then decays rapidly. The decoders, which use β features (Fig. 2.3), should be detecting the β rebound. Previous work has shown how to interact and control robots based on asynchronous decoding on MI vs. rest. In particular, Müller-Putz and colleagues (Mueller-Putz et al., 2010) asked subjects to sustain MI for two different durations, which differed in 2 seconds or more, in order to deliver two different commands. While some subjects could achieve fast transitions for the short-duration commands (1 s), this was not the case for long-duration commands. In our case, subjects started with a stop latency of around 1 s no matter the duration of the MI period. Furthermore, and critically, during closed-loop use subjects in our approach could adapt their self-paced performance to achieve high temporal accuracy. In the discussion of the mentioned paper, authors discuss the difference observed between short and long-duration commands by explaining that a MI pattern cannot be actively stopped by the BCI user. On the opposite, our data shows that a BCI user can learn how to stop these patterns if the paradigm and decoder focus explicitly on MI termination.

2.5 Conclusion

We presented an approach to decode the termination of an imagined movement using both the upper μ and β rhythms. To the best of our knowledge, we are showing for the first time that offset MI decoding has an intrinsic latency mainly due to late appearance of neural correlates of motor termination; however, and critically, this latency can be compensated by BMI users. This compensation is only possible because of the reliability of the decoder as well as the consistency of offset correlates, which makes it possible for users to predict their BMI dynamics. This result also highlights the importance of online evaluation of BMI systems and the implications that closed-loop interactions have in the system performance (Chavarriaga et al., 2017; Perdikis et al., 2018). The natural scenario for detection of MI termination is its combination with detection of MI initiation for natural asynchronous control of neuroprostheses. Such an approach would, for instance, allow users to better control the degree of grasping by exploiting two different but associated MI processes, namely MI initiation and termination.

3 Stopping vs resting state during motor imagery paradigm

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Abstract

Current non-invasive Brain Machine interfaces commonly rely on the decoding of sustained motor imagery activity (MI). This approach enables a user to control brain-actuated devices by triggering predetermined motor actions. One major drawback of such a strategy is that users are not trained to stop their actions. Indeed, the termination process involved in BMI is poorly understood with most of the studies assuming that the end of an MI action is similar to the resting state. Here we hypothesize that the process of stopping MI (MI termination) and resting state are two different processes that should be decoded independently due to the exhibition of different neural patterns. We compared the detection of both states transitions of an imagined movement, i.e. rest-to-movement (onset) and movement-to-rest (offset). Our results shows that both decoders show significant differences in term of performances and latency (N=17 Subjects) with the offset decoder able to detect faster and better MI termination. While studying this difference, we found that the offset decoder is primarily based on the use of features in β ([13-30] Hz) band which appear earlier. Based on this finding, we also proposed a Random Forest based decoder which enable to distinguish three classes corresponding to the three periods of an imaginary movement (MI, MI termination and REST).

3.1 Introduction

A Brain-Machine Interface (BMI) aims at providing communication and control pathways for people with motor disabilities (Millán et al., 2010). This is made possible by enabling users to control external devices and interact with their environment while bypassing the normal neuromuscular pathways. Primarily based on electroencephalogram (EEG), non-invasive BMIs are presented as great instruments to be used in novel forms of therapy such as for stroke rehabilitation (Biasiucci et al., 2018; Daly and Wolpaw, 2008; Dobkin, 2007).

EEG-BMIs are usually based on a well-known paradigm called Motor imagery (MI) which is the process where a person is asked to mentally rehearse a given motor activity without any over motor output (Decety, 1996). While performing MI tasks, changes can be observed in the brain with respect to a resting state. These changes are usually referred to as ERDs (Event-Related Desynchronization) and are characterized by a decrease of power generally observed in μ [8-12] Hz and β [13-30] Hz bands (McFarland and Wolpaw, 2008; Pfurtscheller et al., 2006). For such types of BMIs, users generally follow a training procedure where they are instructed either to perform MI or to not perform any task (resting state, REST). This paradigm is known as a Go/No-Go (GNG) task (Birbaumer et al., 1999). Similarly, this paradigm can also be performed sequentially with a person firstly instructed to be resting followed by an MI task (rest-to-movement transition, onset) (G. R. Müller-Putz, Scherer, Pfurtscheller, et al., 2005).

By exploiting such patterns, a BMI can trigger predefined actions and notably trigger the activation of BMI effectors such as exoskeleton or functional electrical stimulation (FES). However, a major drawback of this decoding strategy is that users are not trained to stop their

actions. Indeed, the MI termination process involved in BMI is poorly understood, most of the studies assumed that the end of an MI action is similar to the resting state, therefore, assuming that it corresponds to the disappearance of MI patterns (Mueller-Putz et al., 2010).

Although this assumption is widely used in the BMI field, the existence of a particular neurophysiological signature observed after movement termination is however well known. This signature can be characterized by an increase of power (event-related synchronization, ERS) induced in the β band. This synchronization, often called β rebound, can last for about a second. Although the role of β rebound is still under debate, it is currently thought to have a function of inhibition of the motor cortex by somatosensory processing (Cassim et al., 2001; Houdayer et al., 2006). Oscillatory activity in the β band has been also linked to an active process to promote the existing motor set aiming to maintain the current sensorimotor or cognitive state (i.e., status quo) (Engel and Fries, 2010). Such synchronizations can be explained by an increase of rhythmic activity paradoxically due to a decrease of the excitability of cortical neurons or inhibited cortical neurons (Pfurtscheller and Lopes Da Silva, 1999; Pfurtscheller and Neuper, 1994). Importantly the presence of β rebound does not require any muscle activation since it was also reported after an imaginary movement (MI task) (Pfurtscheller, 2001). When performing hand-related motor tasks, ERS can mainly be observed in the contralateral hand representation area. In the β band, this synchronization can also be seen in the supplementary motor area (SMA) located in mid-central areas of the brain with slightly higher frequencies and an earlier onset compared to the contralateral ERS (Pfurtscheller, Woertz, et al., 2003; Pfurtscheller, Neuper, Pichler-Zalaudek, et al., 2000).

Neuroimaging studies have also investigated the difference in the motor response inhibition when performing GNG task or Stop-Signal Task (SST) with the last one instructing participants to respond as fast as possible to a stimulus (go trial) but to cancel any response when a stop signal is presented (stop signal). Comparing both tasks, they found notably that these tasks were engaging overlapping but distinct neural circuits with GNG engaging more the frontoparietal control network while SST engages the cingulo-opercular control network to a greater extent, with more pronounced activations in the left anterior insula and bilateral thalamus. Importantly, both tasks also reveal the importance of the anterior insula confirming the role of the SMA (Swick et al., 2011). This last was also found to support both action selection and stopping during a voluntary action (Rae et al., 2014).

In this paper, we investigate the termination process involved during an MI paradigm, and its potential use in BCI applications. We designed a stopping task applied to a MI task by the mean of a clock where subjects are instructed to perform hand MI and stop their MI action as soon as a clock hand is reaching a specific clock tick. The mentioned protocol was tested in offline but also in closed-loop online scenarios.

By doing so, we aim to compare the effect of training a decoder based on the movement-to-rest transition (offset) with the usual decoder trained on the rest-to-movement transition (onset). Here, we hypothesize that (1) the correlates of movement termination during MI tasks are

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different from the resting state, and (2) that such differences can be captured by a BMI decoder which could hence detect faster and better such a transition compared to a usual decoder.

3.2 Methods

3.2.1 Participants

A total of 17 healthy naïve subjects (19-26 years, 8 females, right-hand dominant) participated in the experiment. The study was approved by the Cantonal Committee of Vaud, Switzerland for ethics in human research (CER-VD) and subjects gave their written permission and signed a consent form.

3.2.2 Offline Protocol

The following protocol was adapted from our previous study (Orset et al., 2020). Participants were comfortably seated in front of a PC monitor and asked to perform kinesthetic MI (i.e. imagining the kinesthetic feeling associated with performing a movement) of their right hand while fixating a cross in the middle of a clock shown at the center of the screen. In contrast to our last study, a gauge was added to the design corresponding to a filling green bar and drawn on the clock hand (see Fig. 3.1). This gauge was gradually increasing with time and subjects were instructed to start their MI once the gauge was visible to them. Once this gauge was filled, the clock hand was activated and initiated its turn. The subject was instructed to maintain his MI task and stop his action (MI termination, MIt) only once the clock hand was overlapping with a red target (offset cue) located on a specific tick. The location of this target was varying in time and was uniformly distributed giving a total duration of MI of $4.35s \pm 0.38s$ (mean \pm standard deviation). After terminating their task (MIt), subjects were asked to stay still until the hand clock finishes its turn (4 to 5 s). The total time of a clock hand revolution (MI plus rest) was 8 s. In order to promote correct MI action, subjects were also wearing an exoskeleton hand-induced motion on their right hand. The exoskeleton was designed to actively control the flexion and the extension of all fingers (Randazzo et al., 2018). Importantly, the actuation of this exoskeleton was used only as a feedback and was done once the clocked finished to revolve to avoid any contamination of MI correlates. In between trials, a relax period of 5s was introduced. In total, 4 runs of 20 trials were performed by the subject.



Figure 3.1 – Trial structure during the offline session. During a trial, the subject is asked to continuously look at a fixation cross in the center of the clock. The subject is instructed to stay calm for the first 3 seconds without moving or blinking. Once a gauge represented as a filling green bar is visible, the subject initiates motor imagery (MI) of his right hand. After 2s of MI, the gauge was completed, and the clock hand began his turns around the clock. When the clock hand reaches a target (red bar), the subject should stop motor imagery (MIT) and remain still (no blink or movement) until the clock hand finishes to revolve. A period of 5 seconds following each trial allows the subject to relax.

3.2.3 Online Protocol

An online session was also recorded where participants were actively controlling the clock through the use of a finite state model with a sequential use of two decoders. Both decoders were trained on the offline data (c.f. Section 3.2.6) to respectively detect the onset and the offset transition. Participants' task was to initiate the clock hand and to stop later precisely on a target by controlling their MI action. Each subject performed 4 runs of 15 trials each (60 trials in total). Contrary to the offline protocol, the gauge was changing based on the BMI output of the onset decoder as a source of continuous feedback. This continuous feedback was present only for MI onset detection. Here, BMI output corresponded to the integration of the output probabilities of the decoder to each single EEG sample based on an exponential moving average (Eq. 3.1) (Perdikis et al., 2011). The smoothing parameter α was set by the operator and kept fixed for the rest of the experiment.

$$P(t) = \alpha P(t) + (1 - \alpha) p(t) \tag{3.1}$$

where α is a smoothing parameter, $0 \le \alpha \le 1$, pt is the posterior probability of detecting MI onset and P(t) is the probability obtained after smoothing. Accordingly to the finite state model, once the onset transition was detected, a second decoder was launched and focused on the detection of the MI termination. Here, the detection of MIt was based on an accumulated decision, i.e. counting the number of times the decoder was detecting MIt (p(t) > 0.5). This parameter was set by the operator and kept fixed for the rest of the experiment as well.

3.2.4 Recording System

EEG signals were recorded at a sampling frequency of 512 Hz with 16 active surface electrodes placed over the sensorimotor cortex i.e., on positions Fz, FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4, CP3, CP1, CPz, CP2, and CP4 according to the international 10/10 system (reference: left earlobe; ground: AFz; gtec gUSBamp, Guger Technologies OG, Graz, Austria). The amplifier was set with a hardware band-pass filter between 0.01 and 100 Hz (Butterworth 4th order) and a notch filter between 48 Hz and 52 Hz. A common average reference was used on the EEG raw data to enhance the signal-to-noise ratio.

3.2.5 Analysis of EEG motor correlates

Time-Frequency Analysis

To study the correlates of motor termination, a spectral analysis was first performed on the following six channels: FCz, C3, C4, Cz, CP3, and CP4. We evaluated the event-related spectral changes (ERSP) with respect to the offset transition (Makeig, 1993). The spectrogram was averaged over subjects and was obtained with the following equation (Eq. 4.1):

$$ERD/ERS = 10 * log(\frac{A}{B})$$
(3.2)

Where A represents the power activity computed with the short-time Fourier transform and for a frequency of interest at a given time and B represents the average power during a baseline interval, chosen between [-2,0] with respect to the onset. The average band power was also calculated by computing the average power over μ and β frequency bands using the same baseline.

Statistical Analysis

Statistical analysis was performed on the population level to discern significant ERD/ERS patterns with α = 0.05 on the ERSP maps. To do so, a non-parametric permutation test (n = 5000 permutations) (Graimann et al., 2002) was performed and was corrected for multiple comparisons using max-pixel-based thresholding. A similar test was performed on the averaged band power.

3.2.6 Offline Classification

Training

Two decoders (aiming for onset and offset detection) were trained based on the data from the offline experiment protocol. Power spectral densities (PSD) were computed in a 1s-window based on Thomson's multitaper power spectral density (PSD) estimation from 8 to 30 Hz with a 1 Hz resolution on the 16 channels, yielding a total of 592 features. To assess the classification performance, we performed a nested cross-validation (CV) based on 10 folds where the number of features used to build each model from each fold was fine-tuned. Importantly, these 10-fold were trial-based to avoid any possible overlapping between training and testing sets. For each fold, a diagonal Linear Discriminant Analysis (d-LDA) classifier was trained to distinguish between MI and MI termination processes which were respectively defined between the time intervals [-2, 0] s for MI and [0.5, 2.5] s for MI termination with respect to the offset cue (t = 0). To fine-tune the number of features, inside each fold, we performed an inner 10-fold CV where the number of features was varied between 1 and 50. The optimal number of features was chosen when minimizing the averaged misclassification over the inner CV. Applying a similar process to detect the onset of MI task, a classifier was trained to distinguish between time intervals [-2, 0] s (REST) and [0, 2] s (MI) with respect to the onset (t = 0).

Classification Metrics

To assess the classification performance, we calculated the accuracy at the sample level over the 10-fold cross-validation. Here, one sample corresponds to PSD features estimated on the 1s-window. The accuracy was defined as the number of correctly classified samples over the total number of samples and was computed for each fold. We estimated the chance threshold at the 95% confidence interval based on the inverse binomial cumulative distribution.

Pseudo-online classification

A pseudo-online (PO) analysis was performed on the data to further study the behavior of our offset decoder on the offset transition. In this analysis, the classifier trained to detect the offset transition was tested in the time interval [-3, 4] s with respect to the offset cue. During this time interval, the likelihood for each class was calculated from the decoder on samples computed with a 1s-window shifted every 62.5 ms. Using this decoder, we measured the decoding latency, which we defined as the time when the average posterior probabilities over trials were crossing the chance threshold.

Comparison of decoding approach

For the pure MI task we compare the respective behavior of each decoder when applied in a pseudo-online analysis to detect its own transition (onset PO, offset PO). Through this com-

parison, we compared each decoder type regarding their accuracies to detect MI termination when tested on the interval s [-2, 0] s (MI) and [0.5, 2.5] s (MI termination) with respect to the offset (t = 0) and compare their latency via a pseudo-online analysis in the time interval [-3, 4] s with respect to the offset cue. Importantly, using the onset decoder, the decoding likelihood to detect MI was inverted to obtain the decoding likelihood to detect the rest state while for the offset decoder, the decoding likelihood to detect MI termination was kept.

Random Forest Classification

A Random Forest for the three-class problem was also tested on a 10-Fold cross-validation using the same features as before (see Section 3.2.6) for the three following classes: REST, MI, MI termination. The classifier was trained with 1000 trees with a maximal depth of 5. The features were selected by Random Forest that automatically ranked features based on how they improve the purity of the node. Similarly to Section 5.c, we performed a pseudo-online analysis where we reported the decoding likelihood for each class when an RF-based classifier was tested on a time window [-3, 4]s with respect to either the onset or the offset transition. The alternative to decode both onset and offset transition could bring benefits to the current decoding process as it would decrease the false positive rate. This alternative approach was compared with our previous decoding approach (diagonal LDA + Fisher Score, d-LDA + FS) for the same 3-class problem.

Statistical Analysis

To compare the classification accuracies between the onset and offset classifiers, a paired t-test was used on the mean accuracies per subject. Similarly, a paired t-test was also performed on the average detection over trials. Finally, the average fisher score was also calculated over μ and β bands and averaged over subjects, a paired t-test was also performed on these data.

3.2.7 Post-hoc analysis on online data

Analyzing the online result, three different types of detection were defined based on the time of detection (early detection: < -1.5s, correct detection: [-1.5, 1.5] s, late detection: > 1.5s). To characterize each type, we computed for each type of trials, the fisher score between the sample [-1, 0] s and [-3, -2] s samples.

3.3 Results

3.3.1 Neurophysiological signature of MI termination is different from the resting state

Fig. 3.2 shows the grand average across subjects recorded during pure MI task as well as the power averaged over the μ band [10-14] Hz and β band [20-30] Hz. For each band, we reported the results respectively in blue for the μ band and in red for the β band. When plotting the band powers, we additionally drew horizontal lines to show when an ERS has been found significant based on non-parametric permutation test ($\alpha = 0.05$, repeated measure t-tests based on Wilcoxon rank-sum test, FDR corrected for multiple comparisons). The channels were grouped according to their location on the scalp (central, contralateral, and ipsilateral channels). A significant ERS can be observed in contralateral channels (C3, CP3) as well as for central channel Cz. This increase is mainly characterized in the β band and starts 1s after MI-STOP indicating the presence of β rebound. An increase of power in central channels FCz and Cz can also be observed.



Figure 3.2 – Grand average spectrogram across subjects during the offline session. The vertical lines correspond respectively to the different events in the protocol: starting cue for MI (1st line), the activation of the clock (2nd line), and finally, the stopping cue for MI (3rd line). ERD/ERS were computed with a logarithmic scale using a baseline period [-2 0] s with respect to the starting cue. Below the spectrogram, band power of μ band (in blue) and β band (in red) for each channel averaged over all the trials are shown. The time origin corresponds to the offset. Red horizontal lines on top indicate periods of significant difference for the β band based on the baseline period for its corresponding band ($\alpha = 0.05$, repeated measure t-tests based on Wilcoxon rank-sum test, FDR corrected for multiple comparisons).

BMI for MI termination

We first built two classifiers to detect each motor state transition, namely the rest-to-movement (onset) transition and the movement-to-rest (offset) transition. After that, we evaluated the performances of both onset and offset decoders. For each subject, we reported in Table 3.1 the mean accuracies as well as their standard deviation of the 2-class d-LDA averaged over nested cross-validation and across subjects. On one hand, when decoding the onset, an offline average accuracy was achieved at the sample-based level of $68.0\% \pm 6.4\%$ (mean \pm std). On the other hand, in the case of the offset, an average accuracy of $69.7\% \pm 7.0\%$ was obtained. Importantly, both classifiers decode above the statistical chance threshold (54.17%) for every subject. We reported in Table 3.1 for each subject the latency of their decoder for each transition. In general, one can notice that the onset latency is smaller than the offset latency (paired t-test, t(16) = 4.46, p = 3.9e-04 < 0.001 ***) while the accuracies were not found significantly different (paired t-test, t(16) = 1.05, p = 0.31 > 0.05).

To study the behavior of each classifier during both transitions, we performed a pseudo-online analysis where each decoder was applied in the time intervals [-4, 4] s with respect to the corresponding transition. We can observe a decoding likelihood of MI initiation that seems to reach a plateau which can be interpreted as the detection of sustained MI (Fig. 3.3A) while for MI termination, the decoding likelihood reaches a peak around 2s decreasing rapidly after indicating the detection of a fast and transient state (Fig. 3.3B).

Subject	Onset Accuracy [%]	Onset Latency [s]	Offset Accuracy [%]	Offset Latency [s]
S01	66.9 ± 5.3	0.88	77.0 ± 4.7	1.38
S02	73.6 ± 3.8	1.06	56.6 ± 5.5	2.94
S03	63.5 ± 7.1	1.30	71.4 ± 9.7	1.75
S04	66.5 ± 8.7	0.63	72.5 ± 9.2	1.63
S05	69.6 ± 8.3	1.13	61.7 ± 9.0	1.81
S06	66.3 ± 6.1	1.00	67.5 ± 7.4	1.81
S07	63.3 ± 8.7	1.38	69.5 ± 4.2	1.63
S08	67.8 ± 8.2	1.38	58.6 ± 7.4	1.75
S09	77.7 ± 3.3	1.25	76.5 ± 6.5	1.75
S10	68.4 ± 6.7	0.75	72.3 ± 9.0	1.50
S11	61.5 ± 7.6	1.56	72.2 ± 6.2	1.44
S12	75.2 ± 5.3	1.19	81.6 ± 5.8	1.31
S13	63.6 ± 5.2	1.69	72.7 ± 6.6	1.50
S14	67.8 ± 7.0	0.94	77.4 ± 9.5	1.50
S15	60.2 ± 9.4	0.25	67.8 ± 6.9	1.69
S16	81.7 ± 7.1	0.94	63.2 ± 7.1	0.94
S17	54.8 ± 7.2	0.50	74.6 ± 4.8	1.81
GA	68.0 ± 6.4	1.05 ± 0.38	69.7 ± 7.3	1.66 ± 0.4

Table 3.1 – Classification accuracy for motor state transition decoding. The accuracies and detection latencies were reported for each subject as well in grand average with their mean and standard deviation for both onset and offset decoding.



Figure 3.3 – Grand Average pseudo-online analysis of each decoder on their transition. The likelihood of both decoders averaged over subjects is shown over time. **A**. Pseudo-online decoding of onset decoder applied on the initiation transition (t=0) of MI. **B**. Pseudo-online decoding of offset decoder applied on the termination transition (t=0) of MI. The standard deviation is shown at every time point in grey. The chance level is represented with a horizontal dashed red line.

After building both decoders, we compared each decoder regarding their performances to detect the offset. In Fig. 3.4A, we show the Fisher Score for each feature averaged over subjects and mapped it in 2D (channels x frequencies). On the grand average, when looking at the selected features during the decoding process, both transitions show relevant information on similar spatial locations, i.e. contralateral channels (C3, CP3). However, the features selected for each decoder differ in frequency bands with an onset decoder primarily based on features in the μ band and an offset decoder relying principally on features in the β band. Comparing the average fisher score for both decoder (Fig. 3.4B), we found that μ band was statistically higher for the onset decoder overall channels (paired t-test, t = 3.45, df = 16, p = 0.0033 < 0.01 **). No significant difference was found for β band (paired t-test, t = 0.46, df = 16, p = 0.65 > 0.05).

Then, we compared the decoders regarding their performances to detect the offset transition. In Fig. 3.4C, we reported the accuracies for each subject on the nested 10-fold CV showing an increase of accuracy when applying an offset-specific decoder on the offset transition (69.7% \pm 7.3% for the offset decoder against 61.7% \pm 7.3% for the onset decoder). This increase was statistically tested (paired t-test, *t* = 4.75, *df* = 16, *p* = 2.1e-4 < 0.001 ***). All subjects showed an increase of accuracy using the offset decoder which was significant for 7 of them.

Finally comparing both decoders in a pseudo-online analysis (Fig. 3.4D), we show that the offset decoder can detect the transition faster with an earlier detection occurs at 1.58s \pm 0.36s while using the onset decoder, the detection occurs at 1.97s \pm 0.67s (paired t-test, *t* = 2.67, *df* = 16, *p* = 0.017 < 0.05 *).

Comparing the decoding likelihood of both decoders over the pseudo-online analysis, we also reported a significant difference in the dynamic of the probabilities (non-parametric Wilcoxon rank-sum test, $\alpha = 0.05$, FDR corrected for multiple comparisons). This difference can be explained as our offset decoder detects the β rebound since our decoder was specifically trained on the time interval which exhibits the β rebound. Then our decoder can detect this pattern of motor termination while the onset decoder –not specifically trained to recognize such patternwas detecting only the rest period happening after the β rebound hence explaining the delay in the offset detection.



Figure 3.4 – Comparison between both decoding on MI termination. **A**. Map of selected features averaged over all subjects for each decoding approach. **B**. Average Fisher score over all channels for μ ([8-12] Hz) and β ([13-30] Hz) bands. **C**. Classification accuracies of motor termination by both decoders are reported using boxplot with each dash line representing a subject (green is showing a significant difference of accuracies). **D**. Pseudo-online analysis of the decoding termination averaged over subjects for each decoder. The solid vertical line corresponds to the offset transition and the horizontal dash lines correspond to the time when the decoding likelihood is reaching the chance threshold. Grey rectangles on the top of the plot show a significant period where the onset and offset decoder show a significant difference. These periods were found based on statistical analysis (non-parametric Wilcoxon rank-sum test, $\alpha = 0.05$, FDR corrected for multiple comparison). Boxplot for latency detection was also reported on the bottom right corner for both decoding.

3.3.2 Online Protocol Results

During the online session, subjects were instructed to initiate the clock hand by performing MI, and then, to stop the same clock hand by stopping their MI. In Fig. 3.5, we reported the results of this experiment showing that on the grand average subjects learn to stop the clock hand effectively. Putting all the trials together, we found that on the grand average we found that the BMI was stopping the clock hand with a median of 0.62s [Q1: 0.89s, Q3: 1.87s] (Fig. 3.5A). Following these results, we reported the fisher score before the detection made by the BMI. In results, visual inspection shows that the decision taken from BCI on the

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correct detection interval relies more on β rebound on contralateral channels (C3, CP3) as well as central channel FCz while the late detection will rely additionally on μ features with more contralateralization (Fig. 3.5B). These results support our previous results and reinforce our previous findings on the difference between the correlates of REST and MI termination. Moreover, they show that β rebound allows sharper detection allowing our decoding to be more accurate in time.



Figure 3.5 – Performances during the closed-loop experiment. **A**. Distribution of latency trials for each subject. Each point corresponds to the latency of one trial and was calculated by computing the difference between the time when the participant is supposed to stop and when the clock hand was stopped by BCI. Boxplots illustrate the distribution and the median latency for every subject as well as on the grand average. Colored areas represent the intervals of different detection types (early detection: < -1.5s [blue], correct detection: [-1.5, 1.5] s, late detection: > 1.5s [orange]). **B**. Fisher score map averaged over all subjects. For each detection type (early, correct, late), we computed for the corresponding trials the fisher score between [-1 0] s and [-3, -2] s samples. Fisher scores are shown for the features (channels x frequencies). Higher values (i.e., yellow color) indicate highly informative features while blue colors indicate less informative features. The scores were normalized for each subject using min-max scaling.

3.3.3 Three Class Model

In this section, we investigated the feasibility to decode through a unique decoder both onset and offset transition. We reported the classification accuracies of both approaches in Table 3.2 for each subject. Results indicate that RF can decode simultaneously better both motor state transitions. Indeed, an average accuracy of 48.9% ± 4.4% was found for d-LDA+FS approach while an average accuracy of $58.2\% \pm 5.9\%$ was found for RF corresponding to an almost 10% significant increase (paired t-test, t = 10.570, df = 16, $p = 1.3e-8 < 0.001^{***}$). Confusion matrix averaged over subjects was also reported for RF in Fig. 3.6B showing that RF can reliably decode each state (REST, MI, MIt) above chance level (> 0.3). Similar to the previous analysis, we first looked at the features importance of our classifier. In this case, RF automatically performs feature selection. For each subject, we computed the features importance mapping and averaged it over subjects. In Fig. 3.6A we show the results of these mapping averaged over subjects. Similar to Fig. 3.4A contralateral channels (C3, CP3) are primarily selected by the Random Forest with both μ and β bands carrying relevant information to discriminate the three different classes. Finally, we also performed a pseudo-online analysis on both onset and offset transition using our RF classifier (Fig. 3.6C). Results show a clear period devoted to each of these transitions. Importantly, during the offset transition, the distinction between MIt and Rest is captured by our decoder. By looking at the dynamic of the decoding likelihood, we can strongly conclude that RF relies on β rebound for detecting MIt. Once this rebound is not detected, the rest state follows.

Table 3.2 – Classification accuracy for the three-class problem. Mean accuracies and their standard deviation for each classifier was reported in both methods (diagonal LDA + Fisher Score, Random Forest Classification). This was done for each subject as well in grand average with their mean and standard deviation (SD).

SubjectDiagonal LDA + FSRandom ForestS01 53.9 ± 6.4 62.4 ± 7.8 S02 45.3 ± 5.1 48.9 ± 6.0 S03 54.4 ± 6.8 64.5 ± 10.4 S04 51.8 ± 8.0 57.1 ± 6.2 S05 43.1 ± 6.5 48.2 ± 5.0 S06 46.0 ± 5.3 60.4 ± 5.7 S07 44.8 ± 7.3 53.9 ± 4.5 S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9				
S01 53.9 ± 6.4 62.4 ± 7.8 S02 45.3 ± 5.1 48.9 ± 6.0 S03 54.4 ± 6.8 64.5 ± 10.4 S04 51.8 ± 8.0 57.1 ± 6.2 S05 43.1 ± 6.5 48.2 ± 5.0 S06 46.0 ± 5.3 60.4 ± 5.7 S07 44.8 ± 7.3 53.9 ± 4.5 S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA48.9 \pm 4.4 58.2 ± 5.9	Subject	Diagonal LDA + FS	Random Forest	
S02 45.3 ± 5.1 48.9 ± 6.0 S03 54.4 ± 6.8 64.5 ± 10.4 S04 51.8 ± 8.0 57.1 ± 6.2 S05 43.1 ± 6.5 48.2 ± 5.0 S06 46.0 ± 5.3 60.4 ± 5.7 S07 44.8 ± 7.3 53.9 ± 4.5 S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA48.9 \pm 4.4 58.2 ± 5.9	S01	53.9 ± 6.4	62.4 ± 7.8	
S03 54.4 ± 6.8 64.5 ± 10.4 S04 51.8 ± 8.0 57.1 ± 6.2 S05 43.1 ± 6.5 48.2 ± 5.0 S06 46.0 ± 5.3 60.4 ± 5.7 S07 44.8 ± 7.3 53.9 ± 4.5 S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA48.9 \pm 4.4 58.2 ± 5.9	S02	45.3 ± 5.1	48.9 ± 6.0	
S04 51.8 ± 8.0 57.1 ± 6.2 S05 43.1 ± 6.5 48.2 ± 5.0 S06 46.0 ± 5.3 60.4 ± 5.7 S07 44.8 ± 7.3 53.9 ± 4.5 S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA48.9 \pm 4.4 58.2 ± 5.9	S03	54.4 ± 6.8	64.5 ± 10.4	
S05 43.1 ± 6.5 48.2 ± 5.0 S06 46.0 ± 5.3 60.4 ± 5.7 S07 44.8 ± 7.3 53.9 ± 4.5 S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA48.9 \pm 4.4 58.2 ± 5.9	S04	51.8 ± 8.0	57.1 ± 6.2	
S06 46.0 ± 5.3 60.4 ± 5.7 S07 44.8 ± 7.3 53.9 ± 4.5 S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA48.9 \pm 4.4 58.2 ± 5.9	S05	43.1 ± 6.5	48.2 ± 5.0	
S07 44.8 ± 7.3 53.9 ± 4.5 S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA48.9 \pm 4.4 58.2 ± 5.9	S06	46.0 ± 5.3	60.4 ± 5.7	
S08 43.3 ± 6.1 51.4 ± 6.0 S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S07	44.8 ± 7.3	53.9 ± 4.5	
S09 51.0 ± 4.5 67.3 ± 3.2 S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S08	43.3 ± 6.1	51.4 ± 6.0	
S10 50.2 ± 5.6 56.7 ± 6.8 S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S09	51.0 ± 4.5	67.3 ± 3.2	
S11 50.8 ± 5.1 59.8 ± 5.4 S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S10	50.2 ± 5.6	56.7 ± 6.8	
S12 57.3 ± 6.9 65.8 ± 5.8 S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S11	50.8 ± 5.1	59.8 ± 5.4	
S13 44.2 ± 5.4 57.0 ± 4.6 S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S12	57.3 ± 6.9	65.8 ± 5.8	
S14 53.4 ± 9.0 66.4 ± 5.6 S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S13	44.2 ± 5.4	57.0 ± 4.6	
S15 45.3 ± 8.2 59.5 ± 5.7 S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S14	53.4 ± 9.0	66.4 ± 5.6	
S16 48.3 ± 2.9 55.2 ± 6.7 S17 48.3 ± 5.3 55.2 ± 5.9 GA 48.9 ± 4.4 58.2 ± 5.9	S15	45.3 ± 8.2	59.5 ± 5.7	
\$1748.3 ± 5.355.2 ± 5.9 GA 48.9 ± 4.458.2 ± 5.9	S16	48.3 ± 2.9	55.2 ± 6.7	
GA 48.9 ± 4.4 58.2 ± 5.9	S17	48.3 ± 5.3	55.2 ± 5.9	
	GA	$\textbf{48.9} \pm \textbf{4.4}$	58.2 ± 5.9	



Figure 3.6 – Random Forest for decoding motor state transitions. Three class problems with Random Forest for decoding motor state transition. **A**. Map of features importance ranked by Random Forest classifier and averaged over all subjects. **B**. Confusion matrix averaged over all subjects. **C**. Pseudo-online analysis using Random Forest on both offset (top) and onset transition (bottom). Both transitions are represented at t=0 with a black dash line.

3.4 Discussion

In this paper, our goal was to investigate the differences between the movement termination and the resting state process involved during a motor imagery task from the neurophysiological and brain-machine interface point of view. To do this, we proposed that (1) the correlates of movement termination during a MI task are different from the resting state, and (2) that such differences can be captured by a BMI decoder.

3.4.1 Neurophysiological differences between MI termination and Rest

The EEG signals were first analyzed via a time-frequency analysis which was applied to the three main periods of interest: the resting state period, the MI period, and the MI termination. As expected, the analysis revealed first the MI correlates, i.e. a decrease of power in μ and β band (μ -ERD and β -ERD). On the opposite, the MI termination is predominantly characterized by an increase of power in the β band (β -ERS, β rebound). This synchronization, consistent with the literature, appears around 1s after MI end and is located mainly over the sensorimotor

cortex on contralateral channels. Although less important, an increase of power in FCz can also be observed, which is consistent with the proposed roles of the premotor supplementary area (preSMA) in the process of stopping a voluntary action (Pfurtscheller, Woertz, et al., 2003; Pfurtscheller, Neuper, Pichler-Zalaudek, et al., 2000).

Although this characterization of the termination process involved during a MI task is consistent with the literature, our previous experiments also showed additional correlates. Indeed, in our previous experiment (Orset et al., 2020), the presence of a μ ERS was found to be predominant and more reliable over subjects while here a β ERS is predominant. This strong component of rest was appearing shortly after the termination of MI and was observed until the end of the trial making such correlates strong features for detecting the end of Motor Imagery. Such differences can be explained mainly by the instruction given to the subjects. First, in the previous experiment, subjects were using both hands while here, the use of the dominant hand was asked. Second, in this previous experiment, subjects were asked to perform a repetitive kinesthetic MI while here, subjects were instructed to do continuous MI. These differences could then explain such conflicting results. While the first difference is dominantly influencing the lateralization of MI termination correlates (Pfurtscheller and Neuper, 1997), the second can induce important changes in these correlates (Stancák Jr and Pfurtscheller, 1996). Indeed, while comparing brief and continuous MI, Nam and his colleagues found a duration effect on MI termination correlates. Importantly they showed that μ power was returning to the baseline more quickly in continuous MI task while on the opposite β power was returning more quickly during the brief MI (Nam et al., 2011). This finding supports our results and explains the absence of μ ERS in this study. Importantly, this implies as well that the termination process might differ based on the type of MI which makes it then a critical factor to take into account for detecting MI termination and the creation of BMI models.

3.4.2 Evidence for the use of a different model to detect MI termination

Most MI-based BMI studies aim to detect MI as a sustained activity. Here, we investigated two different approaches: (1) a finite state model composed of two classifiers to detect both motor state transitions i.e. rest-to-movement (onset) and movement-to-rest (offset) transition, and (2) a three-class Random Forest classifier trained to discriminate between the three classes together (MI, REST, and MIt). Using a finite state model, we trained two decoders on the onset and offset transition. By training a specific decoder trained to detect MI termination, we were able to outperform the standardized BMI decoder based on MI and Rest classes. Our decoder shows faster detection and higher accuracy. This improvement rebound phenomenon. Since such a rebound appears earlier than the baseline return of μ power, these features are more suitable to detect MI termination. On the opposite, a standardized BMI for onset detection will principally rely on μ features and will wait for MI correlates to collapse delaying the detection of MI termination. Additionally, using the finite state model in a closed-loop experiment, a predominance of β features can also be noticed for the trials detected within the correct time

intervals while for the late detection additional features in μ band and associated with an idling process (Pfurtscheller, 1992; Pfurtscheller and Neuper, 1994; Pfurtscheller et al., 1996) can be observed reinforcing the importance of β features for decoding MI termination while being timely accurate. Nonetheless the performance of a finite-state based decoding will be bounded by the performance of the MI onset decoder. Using a 3-class model, a difference between resting state and MI termination was also made by the Random Forest classifier. This classifier was trained to discriminate between the three classes (MI, REST, and MIt) altogether by notably outperforming the LDA classifier by almost 10%. Such differences can easily be explained by the approach used by different classifiers where the multi-class LDA we used was partitioning the different classes to have one class against the rest resulting in 3 classifiers and combining the results while Random Forest was considering the three classifiers together. Hence, Random Forest shows evidence that it is possible to discriminate between the three different classes. More importantly, such a decoder can differentiate between rest and MI termination after MI action showing a transient state for MI termination quickly followed by a durable resting state. More RFs, being a fusion of weak classifiers, are also more robust when dealing with less samples.

Altogether, these findings contradict the current belief to use asynchronous onset decoding on (Mueller-Putz et al., 2010) for the detection of the termination process during MI. The two models can be used as alternative solutions of the usual approach aiming to detect the onset transition. More, these alternatives provide more accurate and more precise detection of the termination process involved during a motor imagery task.

4 Effect of exoskeleton on correlates of motor termination for BMIs

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Abstract

Motor Imagery is a task that was largely investigated in the context of non-invasive Brain-Machine Interface (BMI) and particularly in stroke rehabilitation. Here, such therapy relies on the decoding of motor intent from the users allowing them to trigger different effectors (e.g. Functional Electrical Stimulation, Exoskeleton ...) which in terms will help to promote movement and facilitate neuroplasticity mechanisms. Although this approach shows great promises, one remaining challenge with their use is that they also introduce proprioceptive feedback altering the correlates of MI and strongly impacting the control of BMI users. To overcome this limitation, the control can be based on the use of other limbs than the one targeted by the BMI or can be based on the use of other biosignals such as muscle or eye activities. Although this is generally a good solution, it is however unnatural for the user. In this paper, we investigated the use of β rebound, a correlate naturally exhibited and occurring after MI, and explored its use in the context of movement termination for upper-limb movement. To explore this phenomenon, we recorded subjects under two conditions. In the first one, subjects were asked to start and stop their kinesthetic motor imagery in a cue-based protocol inspired by Libet's paradigm. In the second case, subjects were performing kinesthetic motor imagery with the same protocol but this time while wearing an exoskeleton-inducing closedhand motion. In results, we show that although the subject endures a passive movement, the presence of β rebound can still be observed. Importantly its localization seems to differ when subjects wear the exoskeleton since observed mainly in central channels. We show that that the exoskeleton affects the detection of β rebound since the classification accuracy significantly decreases from 70% to 62% (n = 13 subjects) when the exoskeleton exerts passive movement but the time of the detection did not change implying that the exoskeleton although affecting the correlates does not affect the timing of these correlates and hence their detection. This implies that the exoskeleton although affecting the correlates and the performances does not affect the timing of these correlates and hence their detection Our results support that β rebound could be used to detect motor imagery termination in a natural interaction paradigm where the user could control the degree of grasping of their exoskeleton using congruent MI commands, i.e. subjects are asked to perform MI with the same limb targeted by the BMI.

4.1 Introduction

The ability to interact with our environment is inherent to human nature. This capacity is however compromised in the case of people with impaired motor abilities. To solve this issue, one emerging solution is the use of Brain-Machine Interfaces (BMI) (Millán et al., 2010). Among the different paradigms used for non-invasive BMI, Motor Imagery (MI) has been intensively studied during these past years. It is now known as a potential paradigm to help patients recovering after stroke accidents (Daly and Wolpaw, 2008; Dobkin, 2007; Wolpaw et al., 2002). Among the different applications of BMI, rehabilitation therapy based on BMIs has shown a growing interest for patients where traditional therapies were judged ineffective. Here, the principle is to use BMI to excite the affected limb and facilitate neuroplasticity via

proprioceptive feedback. To do that, BMIs are often coupled with effectors such as Functional Electrical Stimulation (FES) (Biasiucci et al., 2018) or Exoskeleton-induced hand motion (Randazzo et al., 2018). By principle, these effectors are actuated if and only if the BMI recognizes the user brain activity as motor intent which then will exert a passive movement on the affected limb (Buch et al., 2008).

When coupling such effectors with BMI, one challenge often encountered is that such effectors may alter the dynamics of the EEG signal itself. Indeed, it was shown that the use of effectors such as exoskeleton-induced hand motion induces proprioceptive and sensory feedback promoting similar patterns used for controlling this kind of device (Mima et al., 1999; Weiller et al., 1996). In response to such effect, numerous solutions have been investigated with notably paradigms where to target the movement of a specific limb, users are asked to imagine the movement of other limbs. In the past, this solution has been implemented diversely; such as for controlling an exoskeleton for passive hand movement by performing left vs right MI hand (Pfurtscheller, Guger, et al., 2000; Tang et al., 2016), feet MI (Vidaurre et al., 2016). More, the design of hybrid BMIs which relies on the combination of EEG signals with other biosignals (G. R. Müller-Putz et al., 2011) such as EMG (Bhagat et al., 2016; Leeb et al., 2011), or electrooculogram (Soekadar et al., 2016; Witkowski et al., 2014) has also been investigated. Although these solutions have shown great success to control BMI effectors, they are also based on a non-natural interaction paradigm hence strongly limiting their use. This is even more critical in the context of rehabilitation therapy since here the natural interaction is crucial in order to promote neuroplasticity mechanisms. Hence, in such context, BMIs are usually based on the triggering of predefined and simple action (e.g wrist extension, closing hand...) greatly limiting the range of movement for the patients.

To deal with this issue, one of the correlates of MI, often neglected for controlling such devices, is the correlate of MI termination, known as β rebound. This phenomenon, observed in both movement execution and imagination (Pfurtscheller, 2001), is characterized by an increase of power (event-related synchronization, ERS) in β band (13-30 Hz) and can last for about a second (Pfurtscheller and Lopes Da Silva, 1999). When performing hand-related motor tasks, ERS can mainly be observed in the contralateral hand representation area. In the β band, this synchronization can also be seen in the supplementary motor area (SMA) located in mid-central areas of the brain with slightly higher frequencies and an earlier beginning compared to the contralateral ERS (Pfurtscheller, 2001; Pfurtscheller, Woertz, et al., 2003). Such synchronizations can be explained by an increase of rhythmic activity paradoxically due to a decrease of excitability of cortical neurons or inhibited cortical neurons (Pfurtscheller, 2001; Pfurtscheller and Lopes Da Silva, 1999). Using this natural phenomenon in the context of BMIs, one interesting application could be to allow BMI users to turn off such an effector which hence could provide finer control. In the past years, this correlate was successfully used as a brain switch (Bai et al., 2007; G. R. Müller-Putz et al., 2010; Pfurtscheller and Solis-Escalante, 2009). However, this switch was only designed in an incongruent way with subjects imagining limb movement that differ from the one wearing the effector (e.g. turning on/off an upper limb exoskeleton by imagining the movement of the feet) (Pfurtscheller, Solis-Escalante, et al.,

2010). Although such decoding strategy has shown success for control-ling BMI effectors, it was also shown that subjects can deliver congruent MI commands (Tavella et al., 2010) with subjects imagining a movement of the same limb that is being actuated by the effector (e.g. through FES). Using such a congruent approach could offer a more natural interaction paradigm critical for daily living BMIs and could be used for rehabilitation therapy to promote more functional movements.

Hence, in this study, our interest was to investigate if such a congruent approach was possible when using correlates of MI termination in the context of upper limb movements BMIs and how these correlates could be used to turn off an exoskeleton. In this scenario, BMI users would be able to actuate a hand exoskeleton based on a MI-based BMI which would induce a passive closing movement of their hand. Then by stopping their MI action and exhibiting correlates of MI termination, they could control when the induced movement should stop which in the term could allow them to control the degree of grasping of such exoskeleton.

To do this, we addressed in this paper the following two questions:

- 1. Can we observe correlates of MI termination while performing MI during movement induced by a hand exoskeleton?
- 2. If such correlates can be observed, can they be used to detect MI termination to stop a hand exoskeleton?

To answer these questions, we designed a task where subjects were asked to perform kinesthetic MI of their dominant hand under two conditions. In the first condition, the subject was instructed to start and stop his action on a cue-based paradigm via a clock. This experiment was performed de novo with the same subjects performing the task while wearing an exoskeleton that passively induces hand motion. In this second condition, the subjects were first asked to initiate their MI which was followed by the activation of the exoskeleton to promote a passive closing-hand movement until the clock finished revolving. During the clock revolution and while still having passive closing-hand movement participants were instructed to stop their MI action.

4.2 Methods

4.2.1 Participants

A total of 13 healthy naïve subjects (19-26 years, 8 females, right-hand dominant) participated in the experiment. The study was approved by the Cantonal Committee of Vaud, Switzerland for ethics in human research (CER-VD) and subjects gave their written permission and signed a consent form.

4.2.2 Offline Protocol

The following protocol was adapted from our previous study (Orset et al., 2020). This study was performed over two sessions (one session per condition with 1-2 months between both sessions). For each session, 4 runs of 20 trials were performed. In the first session (pure MI condition), participants were comfortably seated in front of a PC monitor and asked to perform kinesthetic MI (i.e. imagining the kinesthetic feeling associated with performing a movement) of their right hand while fixating a cross in the middle of the clock. In contrast to our previous study, a gauge was added to the design corresponding to a filling green bar and drawn on the clock hand (see Fig. 4.1). This gauge was gradually increasing with time and subjects were instructed to start their MI once the gauge was visible to them. After 2s and with the gauge filled, the clock hand was activated and initiated its turn. The subject was instructed to maintain the MI task and stop the action (MI termination, MIt) only once the clock hand was overlapping with a red target (offset cue) located on a specific tick. The location of this target (i.e. the MI duration) was varying in time between 3 to 4s. After terminating their task (MIt), subjects were asked to stay still until the hand clock finishes its turn (4 to 5 s). The total time of a clock hand revolution (MI plus rest) was 8 s. In between trials, a relax period of 5s was introduced between trials.

In the second session (MI-EXO condition), subjects were instructed to perform a similar task as in the first condition while this time wearing an exoskeleton passively inducing closing hand motion on their right hand. The exoskeleton was designed to actively control the flexion and the extension of all fingers (Randazzo et al., 2018). Before starting a new trial, the exoskeleton was set to an open-hand position and was activated once the clock hand started to revolve.

At this point, it passively closed the hand of the subject (see Fig. 4.1). Subjects were instructed to continue their MI during the exoskeleton activation and as during the pure MI condition, to stop their MI once the clock hand reached the red target. After that, the subject should remain still until the clock hand finishes to revolve as in the first condition. Importantly, the exoskeleton was not stopped when the clock hand was crossing the red target but continued to passively close the hand of the subjects until the clock finishes to revolve. This yields to the continuation of the passive closing hand movement after having subjects stopped their MI. The rationale of this experimental paradigm was to emulate a closed-loop scenario where, in order to stop the exoskeleton is still actuating a movement. Hence in this MI-EXO condition, three distinct periods can be observed: a period of MI only (MI), a period of MI while the exoskeleton is actuated (MI-EXO).


Figure 4.1 – Experimental Protocol using exoskeleton hand-induced motion. **A**. During a trial, the subject is asked to continuously look at a fixation cross in the center of the clock. The subject is instructed to stay calm for the first 3 seconds without moving or blinking. Once a gauge represented as a filling green bar is visible, the subject initiates his motor imagery (MI) of his right hands. After 2s of MI, the gauge was completed, and the clock hand began his turns around the clock. Here, the exoskeleton is activated once the clock hand starts to revolve. When the clock hand reaches a target (red bar), the subject stops his motor imagery (MIt) and stays still (no blink or movement) until the clock hand finishes to revolve. The exoskeleton is still activated until the clock finishes to revolve. A period of 5 seconds following each trial allows the subject to relax. **B**. Picture shows the setup of the exoskeleton on the subject right hand.

4.2.3 Recording System

EEG signals were recorded at a sampling frequency of 512 Hz with 16 active surface electrodes placed over the sensorimotor cortex i.e., on positions Fz, FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4, CP3, CP1, CPz, CP2, and CP4 according to the international 10/10 system (reference: left earlobe; ground: AFz; gtec gUSBamp, Guger Technologies OG, Graz, Austria). The amplifier was set with a hardware band-pass frequency between 0.01 and 100 Hz (Butterworth 4th order) and a notch filter between 48 Hz and 52 Hz. A common average reference was used on the EEG raw data to enhance the signal-to-noise ratio.

4.2.4 Analysis of EEG motor correlates

To study the correlates of motor termination, a spectral analysis was first performed to analyze the event-related spectral perturbations (ERSP) (Makeig, 1993). In this analysis, the spectrogram was averaged over subjects and was obtained with the following equation (Eq 4.1):

$$ERD/ERS = 10 * log(\frac{A}{B})$$
(4.1)

Where A represents the power activity for a frequency of interest at a given time and B represents the average power during a baseline interval, chosen between [-2,0] with respect to the onset of MI (REST period). Statistical analysis was performed on the population level to discern significant ERD/ERS patterns with α = 0.05 on ERSP maps (Graimann et al., 2002). To do so, a non-parametric test (n = 5000 permutations) was performed and was corrected for multiple comparisons using max-pixel-based thresholding. A similar test was performed as well on the averaged band power where the average activity was calculated in two bands of interest, i.e. μ band [10-14] Hz and β band [20-30] Hz which correspond to the main correlates of MI.

4.2.5 Offline Classification

Training

Power spectral densities (PSD) were computed in a 1s-window based on Thomson's multitaper power spectral density (PSD) estimation from 8 to 30 Hz with a 1 Hz resolution on the 16 channels, yielding a total of 592 features. To assess the performance, we performed a nested cross-validation (CV) based on 10 folds where the number of features used to build each model from each fold was fine-tuned. Importantly, this 10-fold were trial-based to avoid any possible overlapping between training and testing sets. For each fold, a diagonal Linear Discriminant Analysis (diag-LDA) classifier was trained to distinguish between time intervals [-2, 0] s (MI) and [0.5, 2.5] s (MIt) with respect to the offset cue (t = 0). To fine-tune the number of features, inside each fold, we performed an inner 10-fold CV where the number of features was varied between 1 and 50. The optimal number of features was chosen by minimizing the averaged misclassification over the inner CV with the top-N feature selected based on their Fisher Score. The same training approach was used in both conditions (pure MI and MI-EXO tasks).

Classification Metrics

To assess the classification performance, we calculated the accuracy at the sample level over the 10-fold outer cross-validation. Here, a sample is corresponding to a 1s-window. The accuracy was defined as the number of correctly classified samples over the total number of samples and was computed for each fold. We estimated the chance threshold at the 95% confidence interval based on the inverse binomial cumulative distribution. (uniform priors, n = 272 samples in test set), leading to a value of 55%.

Pseudo-online classification

A pseudo-online (PO) analysis was performed on the data to further study the behavior of our offset decoder on the offset transition. In this analysis, the classifier trained to detect the offset transition was tested in the time interval [-3, 4] s with respect to the offset cue. During this time interval, the likelihood for each class was calculated from the decoder on samples computed with a 1s-window shifted every 62.5 ms. Using this decoder, we measured the decoding latency, which we defined as the time when the average posterior probabilities over trials were crossing the chance threshold for the first time.

4.3 Results

4.3.1 Effectors on ERDS mapping

A spectral analysis was performed to analyze how the correlates of MI initiation and termination were affected by the exoskeleton actuation. Fig. 4.2 shows the grand average across subjects recorded during the session. As previously reported a clear ERD pattern appears during the MI period, this desynchronization is enhanced while the exoskeleton is activated and continues during the totality of the trial. An increase of power can be observed on the β band and follows the same dynamic as during the pure MI task. For both conditions and averaged over subjects, we calculated the maximum increase of power in the β band (with respect to the offset cue) during the MIt period and respectively during the MIt-EXO period. Results are summarized in Table 4.1. We fitted a linear mixed effects model with the peak of β bandpower as the outcome variable, with fixed effects of condition (pure MI task, MI-EXO task), channels (contralateral, central, ipsilateral) and their two way interaction including random effect of subject and can be described as follows: Peak_{Power} ~Condition*Channel + (1|Subject-ID).

Results suggests an interaction between the channels and the task condition (F(2,36) = 8.75, p = 0.0008 ***). Post-hoc comparison also shows a significant difference between MI and MI-EXO on contralateral channels (Tuckey HSD, p = 0.0016 ***).



Figure 4.2 – Grand average spectrogram across subjects during the MI-EXO task. The vertical lines correspond respectively to the different events in the protocol: starting cue for MI (1st line), the activation of the exoskeleton (2nd line) and finally the stopping cue for MI (3rd line). ERD/S were computed with a logarithmic scale using a baseline period [-2 0] s with respect to the starting cue. Band power of μ and β band for each channel averaged over all the trials. The time origin corresponds to the offset. Each color bar on the top indicates periods of significant difference with respect to the baseline period for its corresponding band (α = 0.05, non-parametric permutation test with n = 5000 permutations, corrected for multiple comparisons using max-pixel-based thresholding).

Table 4.1 – Power increase across subjects for pure MI and MI-EXO condition. For each subject, the maximum of power in the β band ([13-30] Hz) was calculated with respect to the power at the time of the stopping cue. The mean and standard deviation were reported for the average power over central (FCz, Cz), contralateral (C3, CP3) and ipsilateral (C4, CP4) channels.

Power[dB]	Central (FCz ,Cz)	Contralateral (C3, CP3)	Ipsilateral (C4, CP4)
Pure MI condition	3.9 ± 1.5	5.7 ± 2.8	3.5 ± 1.6
MI-EXO condition	3.3 ± 1.4	3.7 ± 1.5	3.4 ± 1.5

4.3.2 Effectors on Classification Performances

After training a classifier to detect MI termination for both conditions, we show in Fig. 4.3A the Fisher Score for each PSD-based feature averaged over outer cross-validation and subjects (mapping based on a 2D representation channels x frequencies). When looking at the offset transition, one can notice that features are also still located for the majority in the β band.

Although a similar activity can be observed in contralateral channels, one can observe as well relevant features in central channels Cz, C1 over β -high bands between 27-30Hz. This was confirmed while averaging the Fisher score over μ ([8-12] Hz), β -low ([13-15] Hz), β -mid ([16-22] Hz), and β -high ([23-30] Hz) respectively in contralateral (FC3, C3, CP3), central (FCz, Cz, CPz) and ipsilateral channels (FC4, C4, CP4) with a significant difference in β -high on ipsilateral channels (Kruskhal-Wallis One Way ANOVA, p = 0.0034 < 0.01 **, FDR corrected for multiple comparisons) as well as in central channels (Kruskhal-Wallis One Way ANOVA, p = 0.048 < 0.05 *, FDR corrected for multiple comparisons).

In Fig. 4.3B, we reported for each subject the mean accuracies of the outer cross-validation. In the grand average, we were able to detect MI termination with an accuracy of $70.4\% \pm 7.1\%$ when these 13 subjects were performing the pure MI task. This accuracy decreased to $61.7\% \pm$ 7.6% when they performed the same task but wearing the exoskeleton. This difference was found to be statistically significant (paired sample t-test, t = 3.7, df = 12, p = .003 < .01 **). Importantly, in the second condition and despite exoskeleton activation, the classification performances were above the chance threshold of 55% in 11 subjects and 6 subjects showing significant differences in cross-validated accuracies between the two conditions. Additionally to the classification performance, we also performed a pseudo-online analysis on both conditions. We reported the results in Fig. 4.3C, we can observe that the detection threshold is reached at a similar time for both conditions ($t_{detection} = 1.5625$ s) meaning that MI termination was correctly detected even during a passive movement. Additionally to this figure, we also plotted the distribution of the detection time of MI termination for the offset decoder. In pure MI, across these subjects, we found that MI termination was detected at 1.64 ± 0.46 (mean \pm SD) while detected at 1.39 ± 0.65 in the MI-EXO condition. No significant difference was found between the two conditions for the timing of the detection (paired sample t-test, t = 1.35, df =12, p = .25).



Figure 4.3 – Classification results averaged over subjects with exoskeleton movement. **A**. Map of selected features averaged for both conditions (pure MI and MI-EXO conditions). **B**. Boxplot of classification accuracies of motor termination for both conditions. The classification accuracies for each condition regarding the decoding of motor termination are reported for each subject (s1-13) in a boxplot. The dashed line shows the changes of accuracies for each subject. The green dashed lines indicate significant accuracy changes (p<0.05). **C**. Pseudo-online analysis of the decoding termination averaged over subjects for each condition. The solid vertical line corresponds to the offset transition and the horizontal dash lines correspond to the time when the decoding likelihood is reaching the chance threshold. Grey rectangles on the top of the plot show a significant period where the onset and offset decoder show a significant difference. These periods were found based on statistical analysis (non-parametric Wilcoxon rank-sum test, $\alpha = 0.05$, FDR corrected for multiple comparison). Boxplots for latency detection were also reported on the bottom right corner for the offset decoder.

When looking at the classification performances, we observe two distinctive clusters: some subjects seem to be highly affected by the exoskeleton activation exhibiting low decoding performance of MI termination (bad performers, accuracy < 60%, n = 6). Another group of subjects shows relatively good accuracies (good performers, accuracy > 60%, n = 7). Two of these subjects (S11 and S13) present accuracies up to 70%. Looking at these two groups, we

were interested to understand how some subjects seem to be less affected by the exoskeleton while others were strongly impacted. To do this, we computed the Fisher score averaged over each of these groups for the two different conditions and mapped it in 2D (channels x frequencies). For each condition, we reported the feature maps in Fig. 4.4 as well as their topographic map for the respective bands: μ ([8-12] Hz), β -low ([12-15] Hz), β -mid ([16-22] Hz), and β -high ([23-30] Hz). Looking at both feature maps and topoplot, we can observe that during the pure MI task condition, good performers, and bad performers present strong similarities regarding their features mapping since the majority of relevant features are located in contralateral channels such as in C3 and CP3. On the other hand, a clear difference can be spotted in the MI-EXO condition while the bad performers tend to show relevant features in contralateral areas in lower frequencies (β -low, β -mid) and good performers tend to show relevant features in central areas with higher frequencies (β -high).



Figure 4.4 – Group comparison during both conditions. Fisher score maps averaged over subjects for pure MI condition and MI-EXO condition. In this figure, we split into two groups our participants: the bad performer's group (<60% of accuracy, n = 6) and the good performer's group (>60% of accuracy, n = 7) For each group, we show the fisher maps for pure MI condition (left side) and MI-EXO condition (right side). Additionally, to these feature maps, topoplots are showing the topographical mapping of fisher score with respect to the band power: μ ([8-12] Hz), β -low ([13-15] Hz), β -mid ([16-22] Hz), and β -high ([23-30] Hz).

Based on this observation, we computed the average fisher score in β -high frequencies over central (FCz, Cz, CPz) channels. A significant difference was found between good and bad performers on β -high frequencies (Kruskhal-Wallis One Way ANOVA, df = 11, $p = .045 < .05^{\circ}$).

We also calculated the correlation coefficient between these values and the averaged accuracies over the 10-fold nested cross-validation obtained using our decoding approach to detect MI

termination and reported in Fig. 4.5. Based on this analysis, a strong correlation (Pearson correlation coefficient, r = .61, df = 11, p = .027 < 0.05 *) was found for central channels. Note that this correlation was not found when these subjects were performing a pure MI task (r = .18, df = 11, p = .57). Our results suggest that central channels in β -high frequencies are important markers for reliable detection of MI termination when effectors are used in MI-based BMI. Importantly, we also show the correlation for contralateral and ipsilateral channels where no significant correlation was found for ipsilateral channels for pure MI condition (r = .06, df = 11, p = .84) and EXO condition (r = .05, df = 11, p = .84) as expected with hand MI. Note that contralateral channels did not show significant correlation as well although in the pure MI condition, a marginal correlation can be observed (r = .43, df = 11, p = .14) contrary to the EXO condition (r = .25, df = 11, p = .42). Such correlation would be expected in the case of hand MI.

Chapter 4



Figure 4.5 – Correlation between Fisher Score and accuracies. Correlation between Fisher score for contralateral, central, and ipsilateral channels and performance accuracies for MI-EXO and non-EXO (pure MI) conditions. The average Fisher score was calculated and averaged over central channels (FCz, Cz, CPz, see topoplot), contralateral channels (FC3, C3, CP3, see topoplot), and ipsilateral channels (FC4, C4, CP4, see topoplot). The Fisher score for each subject is plotted in function of the accuracies regarding the detection MI termination in both conditions (orange: EXO condition, blue: pure MI condition).

Finally, we looked at the β band power activity between good and bad performers in both conditions (see Fig. 4.6). We observed that good performers had a significant β -ERS in the pure MI condition for contralateral channels (C3, CP3) but also for central channels (FCz, Cz) while the bad performers did not exhibit a significant β -ERS in any of these channels. One can note that for good performers, the β -band power seems to increase and come back to the baseline or higher. This was however not shown significantly above the baseline and could hence not be defined as an ERS with respect to MI onset. It is however important to note that this baseline was defined as a period where the exoskeleton was not activated. In brief, these results show that the central β -high markers which promote a reliable detection of MI termination were already present during the pure MI condition.



Figure 4.6 – Group comparison during both conditions on β -bandpower. Band Power on β band ([13-30] Hz) averaged over subjects for pure MI condition and MI-EXO condition for channels (FCz, Cz, C3, CP3). Participants were split into two groups: bad performers group (< 60% of accuracy, n = 6) and the good performer's group (> 60% of accuracy, n = 7) For each group, we show the β -bandpower for pure MI condition (red) and MI-EXO condition (blue). The time origin corresponds to the offset. The color bar on the top indicates periods of significant difference with respect to the baseline period for its corresponding condition (α = 0.05, non-parametric permutation test with n = 5000 permutations, corrected for multiple comparisons using max-pixel-based thresholding).

4.4 Discussion

In this paper, we showed that β rebound could occur during passive movement while wearing an exoskeleton hand-induced motion. We show that this rebound is similar to the one observed during the pure MI task although more localized in central and ipsilateral channels. More, we show that the presence of β rebound when a BMI effector is used is primordial to be able to detect MI termination. Indeed, we show that such correlates can be used to detect MI termination during a pure MI task and also that a similar dynamic can be observed when subjects are undergoing a passive movement induced by an exoskeleton. Finally, the presence of β rebound in central channels was found as a marker for good performances while performing MI with passive movement induced by the exoskeleton.

4.4.1 Correlates of motor termination during passive movement

When subjects are enduring a passive movement, one can observe that ERS patterns are weakened by the effect of the exoskeleton. Nonetheless, the β rebound can still be observed and occurs at the same time (around 1s) as in the pure MI condition. As a main difference, we observed that this β rebound is not specifically located in the contralateral area but is more prominent in central channels (FCz, Cz) as well as ipsilateral channels (C4, CP4). This difference can be explained notably because of the complexity of the task which promotes predominant activation of the premotor area and then could explain why ipsilateral and central channels were involved in our task (Singh et al., 1998). Indeed, modulation of sensorimotor rhythms is observed when the exoskeleton induces passive movement promoting rhythms mainly in channels less susceptible to be affected. This might also be explained because β rebound is hypothesized to result from a 'cross-talk' of two neural networks in the foot and hand areas which explained why such synchronization is also observed in neighboring cortical areas representing the foot (Pfurtscheller, Woertz, et al., 2003; Pfurtscheller, Neuper, Pichler-Zalaudek, et al., 2000).

4.4.2 Detection of MI termination

Our results show that MI termination is still detectable up to chance level and shows a similar detection time. This implies that the use of the exoskeleton affects the correlates and the decoding performances but does not affect the timing of these correlates and hence their detection. Importantly, we looked at the features that were relevant for the detection of MI termination and showed some differences between subjects. While in the pure MI condition, good performing subjects had their decoder based on β band features and mostly localized on contralateral channels, the relevant features were shifted to the central and ipsilateral side with higher frequencies in β high range when undergoing a passive movement. This allowed reliable detection of MI termination with similar performances to those observed during the pure MI task. The exoskeleton effect has been previously observed during the MI task on the ERD patterns (Randazzo et al., 2018) where subjects performing MI with the same hand which was wearing an exoskeleton (congruent MI). However, this shift was limited to the ipsilateral channels due to the properties of β rebound, the central channels seem even more important for detecting MI termination. Then, we can conclude that decoding MI termination while having a movement induced by the exoskeleton is largely linked to the presence of β rebound in central channels in the pure MI condition and can notably be used as a predictor for BMI performances. Importantly, it is worth noticing that these good performing subjects were already presenting similar patterns in central channels during the pure MI condition but these features were judged less discriminant in the decoding process compared to the contralateral features. On the opposite, because the exoskeleton was largely affecting features

in contralateral channels, central features were mostly selected to detect MI termination. Hence, we can conclude that the change of features observed between pure MI and MI-EXO conditions is not due to an adaptation of a subject to the task but rather constitute a marker already present in pure MI task and which can be used to assess if a person can control the stopping process while using an exoskeleton.

4.4.3 Brain-Machine Interface applications

In the past, few works have studied motor termination, among them, Pfurtscheller investigated the use of a single laplacian electrode in Cz to detect β rebound while subjects were asked to perform brisk foot MI (G. R. Müller-Putz et al., 2010; Pfurtscheller and Solis-Escalante, 2009) to turn on/off a BMI. This approach was later tested to activate a hand orthosis (Pfurtscheller, Solis-Escalante, et al., 2010). Importantly, their work was based on an incongruent approach where feet MI was used to control the activation or deactivation of the hand exoskeleton. This constitutes an important difference with respect to our approach which was based on a congruent approach, i.e. subjects performing MI of the same hand wearing the exoskeleton. To this extent, we can then conclude that the β rebound can be used to detect MI termination while performing also congruent MI tasks. Such an approach would help the user to have better control since it could provide a more natural control with respect to the incongruent approach. This finding reinforces a previous study showing that users can deliver MI commands while having FES stimulation (Tavella et al., 2010) and extend it to the stopping process involved in MI.

In this paper, we show that the presence of these central features in the β -high band can vary from one subject to another one (good versus bad performers). Hence, one interesting question would be to understand why some subjects naturally present such patterns compared to others. More, as it seems to be an important factor when controlling an exoskeleton, the question of how to promote such features is of equal importance. A possible solution that one could investigate is the use of neurofeedback principle and apply it to promote β -high band power for central channels. Such principle was already successfully applied to the Motor Imagery paradigm (Hwang et al., 2009; Omura and Kanoh, 2017) for training BMI users by showing their ERD patterns principally in μ -band with the means of visual (Blankertz, Dornhege, Krauledat, Müller, et al., 2007; Leeb et al., 2006) or auditory (Hinterberger et al., 2004; Nijboer et al., 2008) feedback.

5 Breathing affects motor imagerybased Brain-Computer Interface

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Abstract

A growing literature shows the importance of the physiological system in human behavior. Particularly, respiration has been found to have a key effect on numerous human functions, including, perceptual, cognitive, and motor functions. However, the role of respiratory signals in the field of Brain-Machine Interface (BMI) remains to be clarified. Indeed, the field aiming at providing communication and control pathways for people with motor disabilities is usually rather considering physiological signals as noise. Here, we investigate the effect of respiration on non-invasive BMIs based on Motor Imagery (MI). We focus our analysis on the correlates of MI (Event-Related Desynchronization, ERD in μ [8-12] Hz and β [13-30] Hz bands) as well as on the actual BMI performance. To do so, we design a MI paradigm with phase-locked starting cues linked to the breathing cycle (expiration-locked and inhalation-locked cues) and non-breathing related phase-locked starting cues (time-based cues). After seeing the cue, subjects were instructed to perform a kinesthetic MI task. Results show that phase-locked inhalation cues lead to better performances in MI tasks compared to phase-locked exhalation cues. Moreover, we also show that classical MI correlates, such as μ -ERDs are modulated by the respiratory cycle with stronger correlates observed during late-phase exhalation. Finally, we identify a link between breathing and BMI performance hence proposing breathing signals as a valuable predictor for BMI performance. Our findings highlight the importance of monitoring such signals and more generally presenting the physiological system as a key component of motor preparation and motor imagery.

5.1 Introduction

Brain-machine interface (BMI) is a biomedical signal processing field that has witnessed an impressive expansion in the last few years. This approach aims at providing communication and control pathways for people with motor disabilities (Millán et al., 2010). Using BMI, users can control an external device and interact directly with their environment while bypassing the natural motor pathways. Moreover, using such technology combined with non-invasive neuroimaging techniques such as electroencephalogram (EEG), a novel form of therapy has been showing great promise for stroke rehabilitation (Daly and Wolpaw, 2008) . BMIs are usually based on a well known paradigm called Motor imagery (MI), which is the process involved when a person is asked to mentally rehearse a given motor activity without any over motor output (Decety, 1996). Two main types of MI can be distinguished. In visual imagery (VI), the person is asked to rehearse the movement and visualize it. In kinesthetic imagery (KI), the person is asked to rehearse the movement and better performances, the latter is usually preferred for BMIs (Neuper et al., 2005) even though it is more difficult to perform for naive subjects (Chholak et al., 2019).

Following such paradigms, BMIs are usually trained by associating predefined triggered actions to the detection of specific changes in sensorimotor rhythms and locations that can

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be recorded using electroencephalogram (EEG). As an example, when performing hand MI, changes can be observed in contralateral motor areas over the hand motor regions of the brain and are usually referred to as Event-Related Desynchronization (ERDs). Such patterns correspond to a decrease of power generally observed in μ [8-12] Hz and β [13-30] Hz bands (Pfurtscheller et al., 2006). In these BMIs, only brain signals are usually considered and other biosignals -such as respiratory or cardiac signals- are treated as physiological noise (Pfurtscheller, Ortner, et al., 2010). Despite this assumption, multiple studies have shown that combining such bodily signals to brain signals could improve the reliability of the BMI (Pfurtscheller, Allison, et al., 2010; Shahid et al., 2011). Moreover, BMIs have also shown that these biosignals alone can be used for diverse purposes such as movement detection (Marchal-Crespo et al., 2012) or music imagery detection (Falk et al., 2010).

In addition, new evidence also suggests the importance of monitoring such physiological signals. Particularly, breathing has been found to have a key effect on numerous human functions. Firstly, on a behavioral level, Perl and his colleagues demonstrated that performances during visuospatial tasks with phase-locked inhalation are higher than those with phase-locked exhalation (Perl et al., 2019). This was similarly reported for other cognitive tasks such as visual recognition tasks (Nakamura et al., 2018) or object recognition memory tasks (Zelano et al., 2016). The effect of breathing was also reported on motor functions. Indeed, breathing is synchronized with locomotion in mammals (Bramble and Carrier, 1983). Respiration was recently shown to be coupled with higher-level motor control functions such as voluntary action (Park et al., 2020); the authors reported that the initiation of a voluntary action tends to be in the expiration phase. Secondly, on a neuroimaging level, it has been shown that breathing drives and induces cortical oscillations in multiple regions of the brain such as the olfactory bulb in rodents (Fontanini et al., 2003), the limbic-related brain areas (amygdala, hippocampus) as well as in the piriform cortex in human (Karalis and Sirota, 2018; Zelano et al., 2016). In humans, during a voluntary action; respiratory phases modulate the cortical readiness potential as well; ongoing negativity ob-served on EEG signals preceding self-initiated movements. Such finding suggests again that fluctuations of brain activity are driven by the breathing signals (Park et al., 2020).

Following such findings, one interesting question is to investigate this effect on Brain-Machine Interfaces based, using a Motor Imagery paradigm. Our study aims at investigating how breathing can affect the performances of MI tasks as well as its corresponding correlates using BMI performance metrics and EEG neuroimaging techniques. To do so, we design a MI paradigm with phase-locked starting cues linked to the breathing cycle (expiration-locked and inhalation-locked cues) and a non-breathing related phase-locked starting cue (time-based cues). After seeing the cue, subjects were instructed to perform a kinesthetic MI task.

We hypothesized that phase-locked inhalation cues would lead to better performances in MI tasks compared to phase-locked exhalation cues. Moreover, we hypothesize that classical MI correlates, such as μ -ERDs and β -ERDs would be modulated by the respiratory phases similarly to when performing voluntary action with stronger MI correlates observed during

late-phase exhalation (i.e. cue inhale condition) (Park et al., 2020).

5.2 Methods

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5.2.1 Participants

A total of 34 healthy naive subjects (19-32 years, 18 women, right-hand dominant) participated in the experiment. All participants were compensated for their participation and provided informed written consent in accordance with the Cantonal Ethical Committee of Geneva (CCER) and the declaration of Helsinki (2013).

5.2.2 Protocol

Participants were comfortably seated in front of a PC monitor to perform the task of kinesthetic Motor Imagery (MI). More precisely, participants were asked to imagine the feeling associated with performing a movement of their right hand. The experimental protocol is described in Fig. 5.1. Participants were instructed to stare at a fixation cross during the entire task. Participants were cued by a change of color of the fixation cross indicating the start (fixation cross turning to green) or the end (fixation cross turning to red) of their MI action. In total, participants performed 6 runs of 20 trials. Among these runs, either the starting cue or the stopping cue was based on the respiratory phase (inhalation or exhalation). The respiratory phase was detected in real-time and based on adaptive thresholding. For each run, 10 trials were cued by the inhalation detection while the rest were cued on the exhalation detection. The order of the trials and runs were randomized and a 1s-jitter was added to prevent the subject from anticipating the start of the task. Importantly, when the starting cue was based on the respiratory phase, the stopping cue was time-based on the starting cue and vice-versa. Subjects were performing the MI task during 5s. At the end of each trial, participants were able to relax for a period of 4s. To ensure that participants were unaware of the breathing manipulation, at the end of the experiment, they were asked to reply to the question "According to you, how cues were delivered during the experiment?" by choosing one of the following items: "randomly", "muscle activity", "blinking eyes", "heartbeat", "brain activity", "respiration".



Figure 5.1 – Experimental Protocol. During the experiment, subjects were asked to perform the MI task. The experiment was split into runs with different conditions (respiration-based onset cue or respiration based offset cue). In a run, the trials were split again into two conditions (inhalation-based cue or exhalation-based cue). A trial was organized into different blocks, first, the subject was asked to remain still and wait for the cue to turn green. Importantly, a jitter of 1s was added to prevent the subject from anticipating the cue. Once the cue turned green, the subject was instructed to perform the MI task and to stop MI when the cue turned red. Once the cue turned red and that the subject stopped the MI task, she/he was asked to remain still during 3s while continuing to fix the fixation cross. This was followed by a rest period of 4s during which the participant could move or blink.

5.2.3 Detection of respiratory phases in real-time

Respiration data were recorded using a respiration belt (Piezo Film Effort Sensor – Kit 1389) placed on the abdomen of the participants. Such data were collected in a 10s buffer (> 2 breathing cycles). A Butterworth filter was used to band-pass filter the breathing data between [0.01 - 10] Hz. From this 10s buffer, a threshold was set to 25% of the maximum amplitude for inhalation detection or 25% minimum amplitude for exhalation detection (Eq. 5.1). The maximum and minimum were updated every 62.5ms.

$threshold_{inhalation} = 0.25 * max_{buffer}$	(5.1)
$threshold_{exhalation} = 0.25 * min_{buffer}$	(3.1)

The last time point was then compared to the two thresholds which in results triggered the cues.

5.2.4 EEG Acquisition

EEG signal was acquired thanks to an EEG system with 64 passive electrodes (standard 10/10 system, ANTneuro). EEG signal was first band pass filtered between 1 and 40 Hz. Independent Component Analysis was also performed to decompose the EEG signal into independent component. The IC component originated from eyes artifact were removed and the signal was then reconstructed using only the selected IC component. A spatial filter was finally applied based on Common Average Reference (CAR).

5.2.5 ERD/S computation

A spectral analysis was performed to compute the event-related spectral perturbations (ERSP). In this analysis, the power was calculated with the following equation (Eq. 5.2) and averaged over subjects:

$$ERD/ERS = 10 * log(\frac{A}{B})$$
(5.2)

Where A represents the power activity for a frequency of interest at a given time and B represents the average power during a baseline interval, chosen between [-2, 0] with respect to the starting cue.

A topographic map was plotted for each frequency band of interest: μ [8-12] Hz and β [13-30] Hz.

5.2.6 Post-hoc Respiratory Phase

Respiration data were band-pass filtered between [0.01 -10] Hz. The respiratory phase was calculated by applying a Hilbert transform and taking the angle of the complex argument. For the phase coupling analysis, the respiratory phase was binned into six equally sized bins.

5.2.7 Respiration rate changes

Using the respiratory filtered signal, the respiration rate (RR) defined as the number of breaths taken per minute was computed for each subject. For each subject, the RR was averaged over the two time intervals: one between [-2, 0] s and the other between [1, 3] s with respect to the onset of MI task and respectively representing the REST and MI periods. Finally, the RR change (Δ RR) between those two periods was calculated as follow:

$$\Delta Rr = RR_{Rest} - RR_{MI} \tag{5.3}$$

With RR the number of respiration cycles per minute. From these data, we calculated the interquartile range (IQR) as well as the first and third quartiles (Q1, Q3) and removed outliers if Δ RR was not within [Q1 - 1.5 * IQR, Q3 - 1.5 * IQR].

5.2.8 Phase coupling Analysis

To perform phase the coupling analysis, a zero-phase bandpass was applied to each channel within [8-12] Hz for μ band and within [13-30] Hz for β band. From the filtered signals, a Hilbert transform was applied to extract the envelope of the signal. From such an envelope, the power was computed for each channel from which we subtracted the average power over a baseline interval chosen between [-3, -1] s with respect to the onset. The average power was calculated over the 15 selected channels (Fz, FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4, CP3, CP1, CP2) corresponding to the electrodes of interest for MI tasks. The data were then epoched and the z-scores normalized over the trials. Two time intervals (between [1, 4] s and [-3, -1] s) were chosen to represent respectively the period of MI and REST. From each trial, the respiratory phase was computed for each time point. The band power of μ and β bands were averaged over all the time points and grouped in the same bin of the respiratory phase on these given intervals. Additionally, a topographic map was plotted for each frequency band of interest (μ [8-12] Hz and β [13-30] Hz) with respect to the binned respiratory phase. For each subject, the modulation index was calculated on average over trials for each permutation. This modulation index is a measure that quantifies the deviation of a defined amplitude distribution from a uniform distribution (Tort et al., 2010). Then, the modulation index of each subject was averaged to obtain a grand average modulation index.

5.2.9 Decoding Analysis

Feature extraction

Power spectral densities (PSD) were computed in a 1s-window based on Thomson's multitaper power spectral density (PSD) estimation from 8 to 30 Hz with a 1 Hz resolution on the 15 channels of interest, yielding a total of 345 features.

Cross-validation Process

A nested cross-validation (CV) based on 5 folds in which the number of features used to build each model from each fold was fine-tuned. Importantly, these 5-folds were trial-based to prevent samples overlapping between training and testing sets. Trials were split into different folds based on their chronological order. For each fold, a diagonal Linear Discriminant Analysis (diag-LDA) classifier was trained to distinguish between the two time-intervals [-2, 0] s (REST) and [1, 3] s (MI) with respect to the onset cue (t = 0). The time interval of the MI class was set based on the latency of MI correlates.

Feature selection

To fine-tune the number of features, inside each fold, we performed an inner 5-fold CV in which the number of features varied between 1 and 50. The optimal number of features was chosen when minimizing the averaged misclassification over the inner CV. The features were selected based on the amount of information they provided to discriminate between the two classes. This was computed using the Fisher Score (Bishop, 2006).

Classification Metrics

To assess the classification performance, we calculated the accuracy at the sample level over the 10-fold cross-validation. Here, a sample corresponds to a 1s-window. The accuracy was defined as the number of correctly classified samples over the total number of samples and was computed for each fold. The True Positive Rate (TPR) for Motor Imagery was also computed, such measure corresponds to the number of correct detections within the MI class.

5.2.10 Statistical Analysis

Paired sample t-test

To compare BMI performances between inhale-locked cues and exhale-locked cues, the average accuracies of the 5-fold models were calculated for each subject and each type of cue. A paired sample t-test was then performed comparing all the average accuracies for inhale-locked cues and exhale-locked cues.

Regression and Correlation

After calculating ΔRR on a trial-based level, we computed the average ΔRR over trials for each subject. Using the BMI performances obtained from the non-phase locked cues, we also calculated the average BMI accuracies for each subject. We then performed a linear least regression on the average BMI accuracies with the average ΔRR as a predictor. We then computed the frequentist Pearson correlation coefficient between such variables.

Permutation test

For each subject, the band power for each bin and trial were randomly permuted (N=1000). For each permutation, the modulation index was calculated. Based on the 1000 permutations, a distribution of the modulation index was found and averaged over subjects. This distribution was compared with the real grand average modulation index. A p-value was calculated from this comparison.

Bayesian Analysis

To reinforce the interpretation of our results, we performed Bayesian Paired Samples t-tests and Bayesian correlations, using JASP software (version 0.13.1.0). For each test, we reported the Bayesian factor (BF10). Having a BF10 value smaller than 1/3 indicates substantial evidence supporting the null hypothesis (H0) while a BF10 value greater than 3 is considered as substantial evidence supporting the alternative hypothesis (H1). A BF10 value between 1/3 and 3 means that the data is insensitive, and that more data are needed to conclude.

Mediation Analysis

To investigate the effect of change of respiration rate (Δ RR) on the classification accuracy, a mediation analysis was performed on our data. In this model (see Fig. 5.6 in Supplementary section), we investigate whether μ and β band power mediated the relationship between Δ RR and classification accuracy. We estimated: (1) the total effect of Δ RR on classification accuracy (path c); (2) the direct effect of our model mediated by μ and β band power (path c'11); and (3) the indirect effect of the model (paths a11b11, a21b12). Models were tested using the approach proposed by Preacher and Hayes that allows simple and multiple mediators to be included in the analysis (Preacher and Hayes, 2008). First, classic mediation criteria were tested : (1) The predictor predicts the outcome - path c; (2) The predictor predicts the mediator – the path a; (3) The mediator predicts the outcome while controlling for the predictor - path b (Baron and Kenny, 1986). Finally, the statistical significance of the direct and indirect effects was estimated using a bootstrapping method. To avoid biased estimations under conditions of non-normality, bias-corrected confidence intervals (95%) were obtained with 1000 bootstrap resamples.

5.3 Results

5.3.1 Respiration phase is coupled with neural correlates of MI

We performed spectral analysis, when participants carried out the task (t=0 defined as the MI onset; Fig. 5.2A) and topographic mapping of μ -band average over time. This was done for the MI period (t = [1, 4] s) and the REST period (t = [-3, -1] s). Data were averaged over subjects and revealed a decrease of power (ERD) in μ band over channels contralateral to the hand involved in MI during the task (i.e. C3, CP3). Next, we performed phase coupling analysis to study whether the respiratory phase influences the strength of these fronto-central μ -ERD previously associated with MI. This analysis revealed that these patterns observed during the MI period ([1, 4] s) were modulated by the respiratory phase (see Fig. 5.2B). Using a permutation test on the Modulation Index , we found that the breathing phase was coupled with μ power activity and that a stronger desynchronization occurred during the late phase of exhalation (120°-180°; p = 0.038 < 0.05, N = 1000 permutations, see Fig. 5.2C). As a control, the same analysis was also performed on the REST period (t = [-3 -1] s with respect to onset

cue, see Fig. 5.7 in Supplementary Section). This analysis showed that the rest period was not modulated by the respiratory phase (p = 0.495, N = 1000 permutations, see Fig. 5.7C in Supplementary Section).



Figure 5.2 – Respiratory phase coupling analysis for μ power activities. **A**. Topographic maps of μ averaged over all subjects and over time. The μ power activity ([8-12 Hz]) was averaged over a REST period (t = [-3, -1] s) and over a MI period (t = [1, 4] s). The power was calculated over a 1s window with an overlap of 0.5s. **B**. Topographic maps in function of the respiratory phase for band power over MI period. The band power was calculated for each channel for the 6 equally sized bins of the respiratory phase (x-axis). From the band power, a topographic map was represented for the μ power activities during a MI period [1, 4] s. The average band power of 15 EEG channels (see topoplot on the left bottom corner) of interest was calculated for each subject (time point). The mean over subjects was reported on the figure (blue color) with the horizontal line representing the standard error. **C**. Results of permutation test performed on the Modulation Index. The ground truth Modulation Index was calculated over the average grand power of each subject (red horizontal line). By performing N=1000 permutations on these data, the distribution was found and reported on the plot. The p-value indicated below the red line indicates the percentage of samples superior to the ground truth MI.

These data show that the breathing phase affect the power activity in the μ band influencing the strength of ERD patterns, which are identified as the correlates of MI. In the next section, we investigated whether breathing impacts BMI performance.

5.3.2 Respiration rate is correlated with BMI accuracy

We next investigated another commonly known breathing variable, namely the respiration rate (RR), and studied how the changes in RR influence the decoding of MI periods from those of REST. To do so, we first trained our models to detect MI on the starting cue of the MI task (see Section 5.2.8). These cues were not based on our phase detection algorithm but were set randomly using a jitter. By performing our decoding analysis in this way, we detected MI periods with an accuracy of $62.2\% \pm 5.8\%$ (mean \pm SD; grand average of the 34 subjects, independent of RR). In Fig. 5.3A, we report the average fisher score of each feature in a 2D map (channels x frequencies), revealing that μ and β features in contralateral channels, especially C3 distinguished MI from REST, compatible with the results of the previous spectral analysis Fig. 5.2A.

Calculating the average fisher score over μ and β bands, we found that the μ -band was significantly correlated with decoding accuracy (r = -0.53, p = 0.002, BF10 = 25.8) as well as the β -band (r = -0.82, p = 5.9e-9, BF10 = 2.27e6). These correlations were significantly different (Fisher Z- transformation, z = 2.25, p = 0.02) revealing that the BMI accuracy correlated more strongly on β -band features.

Using these data, we next investigate the relationship between BMI performance (i.e. classification accuracy) and changes in RR, a linear relationship was found between these two variables meaning that the decoding performance could be accurately predicted from the breathing rate changes (Δ RR) by the following formula (see Fig. 5.3B): *accuracy* = 0.6 + 0.73 * Δ RR.

The relationship between the decoding performance and (Δ RR) were positively correlated (r = 0.53, df = 31, p = 0.002 < 0.01, BF10 = 21.05) showing that stronger changes in BR were associated with better decoding performance (see Fig. 5.3B).





Figure 5.3 – Performances on the randomized onset cue of MI. **A**. Feature mapping on randomized onset cue averaged over all subjects. Fisher scores are shown for the features (channels x frequencies). Higher values (i.e., yellow color) indicate highly informative features while blue color indicate fewer discriminant features. The scores were normalized for each subject using min-max scaling. **B**. Classification performances in function of respiratory rate changes between REST and MI period. Each point corresponds to the cross-validated accuracy of one subject in function of the averaged respiratory rate changes calculated between REST and MI period. A regression model was fitted to these data with x as the respiratory rate changes and y as the classification accuracy. The blue line shows this model while the blue shade represents its standard deviation.

These decoding data show that breathing affects BMI performance, hence, the monitoring of breathing signals can be used to evaluate BMI abilities. In the next section, we intended to further analyse this relationship by introducing the neural correlates during MI as possible mediators of the observed effect.

5.3.3 Mediation effect of β power

Meditation analysis was performed on the data to investigate if the neural correlates of MI could mediate the relationship between breathing and BMI performance (see 5.4). A schematic representation of the results showing unstandardized regression coefficients is depicted (see Fig. 5.6) in Supplementary Section).

Results indicated that β bandpower was significantly predicted by Δ RR (path a21; β = -1.59, p = 0.0013 < 0.01, 95% CI [-2.5, -0.67]). The regression coefficient was not statistically significant for μ bandpower (path a11; β = -1.48, p = 0.09 > 0.05, 95% CI [-3.2, 0.26]). β bandpower was also a significant predictor for classification accuracy controlling for Δ RR (path b21; β = 0.38, p = 2e-6 ***, 95% CI [-0.51, -0.25]) while μ bandpower was not able to predict it while controlling for Δ RR (path b11; β = -0.008, p = 0.84 > 0.05, 95% CI [-0.08, -0.07]). Estimated indirect effects (i.e., path a11b11, a21b12) further demonstrated that β bandpower was the only significant mediator between Δ RR and classification accuracy (path a21b12; bootstrapped estimate = 0.56, SE = 0.20, p =0.012, 95% CI [0.19, 1.01]); path a11b11; bootstrapped estimate = 0.014, SE = 0.10, p = 0.85 > 0.05, 95% CI [-0.137, 0.357]). Finally, we estimated the direct effect of

 Δ RR on classification accuracy, controlling for μ and β bandpower as a mediator (i.e. path c11). The regression coefficient was not found statistically significant (path c11, β = 0.16, SE = 0.17, p = 0.37 > 0.05, 95% CI [-0.20, 0.51]). These results support a mediation effect of the β bandpower. Importantly, after controlling β bandpower, Δ RR was no longer found as a significant predictor of classification accuracy. No mediation was observed for the μ bandpower. This absence of mediation for μ bandpower can be explained with the feature maps in Fig. 5.3A where visual inspection shows most of the relevant features located in the β band. As a control, the total effect of Δ RR on classification accuracy was also estimated (i.e. path c). With no mediators in the model, the regression coefficient was found statistically significant (path c, β = 0.73, p = 0.002, 95% CI [0.29, 1.17]). These results are in line with our last results.



Figure 5.4 – Mediation model plot. The graph shows the parameter estimates found by the model (a11, a21, b12, b11, c11). The solid line represents the direct effect between the respiratory changes (Δ RR) and the classification accuracy. The dashed line corresponds to the indirect effect with μ and β band power computed over the MI interval [1, 3] s with respect to the starting cue as mediators. The green color indicates a significant effect while the red indicates a non-significant effect.

In summary, this section further studied our last finding where breathing was found to affect the BMI performance. Here, we show that breathing is primarily affecting the strength of MI correlates which in terms has an impact on the BMI performances.

5.3.4 Exhalation during the task is associated with improved MI detection

To further analyze the relationship between BMI control and breathing, we investigated the effect of breathing on MI performances . For this we compared trials when the onset trigger was either linked to inhalation or exhalation (breathing phase-locked onset cues) (Fig. 5.5A). By triggering the onset of MI task with their breathing phase, we ensured that subjects performed MI task in half the trials during the inhalation (MI INHALE condition, $221.2^{\circ} \pm 36.8^{\circ}$) and the exhalation phase (MI EXHALE, $135.8^{\circ} \pm 39.4^{\circ}$; see Fig. 5.8 in the Supplementary Section). Note that subjects were not aware that the triggers were delivered related to the breathing cycle (see Fig. 5.9 in the Supplementary Section). The proportion of subjects who reported that the cues

were random was found significantly different from a random distribution ($\chi^2(1,34) = 52.5$, p = 4.3e-10). This suggests that the subjects did not seem to be aware of the objective of the experiment.

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For both conditions, a model was trained and evaluated with the True Positive Rate (TPR). Additionally, we reported feature mapping averaged over subjects (see Fig. 5.10 in Supplementary Section). Considering the grand average, these data revealed that subjects performed better MI during the exhalation phase than during the inhalation phase. Thus, we found that the TPR differed significantly and was $60.8\% \pm 14.5\%$ during MI INHALE condition while being $63.6\% \pm 14.7\%$ for the MI EXHALE condition (Fig. 5.5B; paired sample t-test, *t* = 2.16, *df* = 33, *p* = 0.038 < 0.05, *BF10* = 1.4). Although significant, the reported Bayesian Factor (1 < BF10 < 3) implies that even though frequentist statistics show an effect, the Bayes factor suggests more data are needed to conclude a difference of performance between inhalation and exhalation cue. However, this result seems to be consistent with Fig. 5.2B showing stronger MI correlates during exhalation, and particularly during its late phase



Figure 5.5 – Performance comparison between inhalation and exhalation onset of MI task. **A**. Detection of inhalation and exhalation for cueing MI task. The left panel shows the amplitude of respiratory signals. The line represents each subject averaged respiratory activity across trials (blue: exhale starting cue, orange: inhale starting cue). The dashed vertical line represents the time when subjects are instructed to start their motor imagery. The grey and green rectangles correspond to the time interval representing the REST and MI classes, respectively, during the decoding process. **B**. The scatter plot represents the average cross-validated decoding performances built on the inhale cue in function of the one obtained from the exhale cue. The decoding performances are assessed with the true positive rate of the MI class (i.e. the number of correct detections within MI class).

In summary, this section suggests that breathing impacts the BMI performance with a difference in BMI accuracies when MI is performed under different respiratory-phase conditions (inhale or exhale). This effect is associated with a change of power in μ -band indicating again an effect of breathing on MI correlates and BMI performances.

5.4 Discussion

In this paper, we investigated how breathing can affect Brain-Computer Interfaces based on a Motor Imagery paradigm. We show evidence that phase-locked inhalation cues lead to better performance for MI tasks compared to phase-locked exhalation cues and that MI correlates are modulated by the respiratory phases. Our analysis focused mainly on the correlates of MI corresponding to a decrease of power in μ and β bands (μ -ERD and β -ERD) and was observed in EEG electrodes over the contralateral cerebral hemisphere. First, we investigated the effect of breathing on MI correlates and on BMI performances from the model we trained on these features. We show that the MI correlates are affected by the respiratory phase with particularly μ -ERD showing a stronger power in the late expiration phase. This is comparable to effects reported in the case of voluntary movement showing a modulation of the cortical readiness potential or RP (Park et al., 2020). Although both datasets (RP and BMI) found a modulation by the respiratory cycle, a RP amplitude was found smaller during expiration (compared to the inhalation; RP data), our study reported stronger μ -ERD during the late expiration phase. We argue that this difference is likely explained by the fact that MI corresponds to an imaginary movement (that shares many similarities with an executed movement) while RPs are found prior to an executed movement and are involved in the initiation of a movement (Shibasaki and Hallett, 2006). Accordingly, μ -ERD and RP are inherently different and sequential signals involving different brain regions -RP localized in prefrontal regions involving the supplementary area (SMA) and MI, related μ -ERD localized in contralateral premotor and motor cortex, (as movement execution (Miller et al., 2010). Because of such differences in the signal signature, the analysis on the RP datasets was performed on time intervals prior to the movement onset while our analysis was performed after MI onset.

Second, we show that the changes in respiration rate during the task predict BMI performance, making breathing a reliable indicator regarding BMI ability. Breathing related signals have previously been used to distinguish action success from action failure in several tasks, such as shooting (Deschaumes-Molinaro et al., 1991), indicate sports performance (Collet et al., 1999), or to distinguish between elite and non-elite athletes (Oishi and Maeshima, 2004). The present data on respiration rate and BMI performances show this effect for the first time on BMI performance.

Mediation analysis showed that the change of respiration rate has an indirect effect on BMI performance and was mediated by the power of β -ERD. This reinforces previous proposals that activity of the autonomic nervous system related to breathing control impacts action control and BMI control (Collet et al., 2013). Importantly, while in the mentioned studies, the authors found a higher increase of respiratory rate as an indicator of high performances, this inverse relationship was found in our study: a larger decrease of respiration rate corresponding to higher performances. It is worth to note that this difference could be explained as in these studies MI tasks were performed during a longer period of time (minutes) (Oishi et al., 2000) while being performed during few seconds in our study.

Third, our results suggest that higher BMI performance is phase-locked to inhalation, corroborating previous studies in visuospatial tasks (Perl et al., 2019), visual recognition tasks (Nakamura et al., 2018) or in object recognition memory tasks (Zelano et al., 2016). These latter results were not supported by Bayesian analysis (indicating the necessity to collect more data), however, they do corroborate our first finding showing that the subjects are performing better MI during the expiration phase. Performing a source localization on the data used to train our BMI models, we found that the difference of power on μ band was significantly correlated with the difference observed in BMI metrics. Such correlation is another element supporting the hypothesis of an effect of breathing on BMI performances.

In conclusion, our results show that breathing impacts several key human functions, including the control of a BMI. Our data show that respiration affects MI-based BMIs and their performance. More importantly, our data shows that breathing is a reliable indicator for BMI performances and then should be closely monitored. Therefore, we argue that breathing should be considered in the design of future BMIs, to foster MI correlates and improve BMIs' accuracy.

5.4.1 Supplementary Materials



Figure 5.6 – Schematic representation of the mediation model of interest. This schematic shows the direct effect of Δ RR on the classification accuracy (c11) of the model mediated by μ (8-12 Hz) and β (13-30 Hz) bandpower and the indirect effect of the model (paths a11b11, a21b12).



Figure 5.7 – Respiratory phase coupling analysis for μ power activities during REST. **A**. Topographic maps of μ averaged over all subjects and over time. The μ power activity ([8-12 Hz]) was averaged over a REST period (t = [-3, -1] s) and over a MI period (t = [1, 4] s). The power was calculated over a 1s window with an overlap of 0.5s. **B**. Topographic maps in function of the respiratory phase for μ band power over MI period. The band power was calculated for each channel for the 6 equally sized bins of the respiratory phase (x-axis). From the band power, a topographic map was represented for the μ power activities during a REST period [-3, -1] s. The average band power of 15 EEG channels (see topoplot on the left bottom corner) of interest was calculated for each subject (time point). The mean over subjects was reported on the figure (blue color) with the horizontal line representing the standard error. **C**. Results of permutation test performed on the Modulation Index. The ground truth Modulation Index was calculated over the average grand power of each subject (red horizontal line). By performing N=1000 permutations on these data, the distribution was found and reported on the plot. The p-value indicated below the red line indicates the percentage of samples superior to the ground truth MI.





Figure 5.8 – Circular distribution of samples during MI class for each starting cue type. The time interval of MI class corresponds to [1 3] s with respect to the starting cue. In this histogram, we plotted the distribution for all the subjects of the samples from each trial.



Figure 5.9 – Results of the post-hoc questionnaire. Participants were asked to give their opinion on how the cues were triggered during the experiment. Different choices were given to them: randomly, muscle activity, blinking eyes, heartbeat, brain activity, respiration. The bar plot represents the results of the questionnaire and shows the number of people in function of the different options suggested in the questionnaire.





Figure 5.10 – Feature mapping for inhalation and exhalation starting MI cue across subjects. Fisher scores are shown for the features (channels x frequencies). Higher values (i.e., yellow color) indicate highly informative features while blue colors indicate fewer discriminant features. The scores were normalized for each subject using min-max scaling. The plot on the left bottom corner indicates the significant difference on each feature between the inhalation and exhalation cues (non-corrected repeated t-test, green: p < 0.05, yellow: p < 0.01). On the bottom right, the t-Score was reported for each feature.

6 General Discussion

6.1 Achieved results

This thesis focused on the use of EEG correlates of motor imagery (MI) while considering MI not as a sustained motor task but rather on its motor state transitions that distinguish the initiation and the termination. I focused particularly on the termination of upper limb movements for more natural and intuitive BMI interactions and investigated the use of this approach aiming to decode the stopping process occurring after MI. Through this thesis, I investigated the different components of our approach considering SMR in μ and β bands. I studied how its use within the field of BMI could be done by investigating at (i) the feasibility to decode motor termination from the neural correlates of motor termination with, notably, the use of the β rebound in BMI and studied how BMI users could learn to module these correlates in closed-loop scenarios. I also determined (ii) the benefits in term of performance and latency to use motor termination correlates with respect to classical correlates of MI, and (iii) the effect on the correlates of motor termination when users are confronted with BMI effectors. In a final, fully experimental, BMI project (iv), I investigated how respiratory signals, which have an inherent link to motor processes, can affect the correlates of MI and how monitoring these signals could enhance BMI performance.

The research presented in *Chapter 2* investigated the decoding of motor termination during an imaginary task (MI termination) in a closed-loop experiment. In summary, this study shows that the use of the neural signature of MI termination leads to an intrinsic latency in the decoding of motor termination which can be compensated by BMI users during closed-loop scenarios. This compensation is possible only due to reliable decoding allowing the user to predict their BMI dynamics. Hence, using such an approach, BMI users can control the interruption process of their interface.

The research presented in *Chapter 3* investigated how BMI users could benefit from the approach based on motor state transition with respect to a more classical approach trained to distinguish a period characterized by sustained MI from a period of rest. In summary, this study shows that the decoding of MI termination based on the correlates of motor termination

(β rebound) not only shows a significant increase in BMI performances but also allows a faster detection of the stopping process. Additionally, two solutions were explored for the integration of such a module within standard BMIs which consist of (1) either using a finite state machine combining the decoding of both onset and offset transition or (2) either to use a three-class model trained to distinguish the three different periods, i.e. resting state, MI, and MI termination.

The research presented in *Chapter 4* tackles the use of BMI effectors such as an hand exoskeleton in closed-loop operation for motor termination. In summary, the study shows that the use of an exoskeleton was affecting the correlates of motor termination which is likely explained by the exoskeleton inducing proprioceptive and sensory feedback (Mima et al., 1999; Weiller et al., 1996) which in terms promote similar patterns used in the control of BMIs. However because of this effect was contained on contralateral channels and, because of the cross-talk property of the β rebound, the presence of β rebound was observed over central channels with higher frequencies (Pfurtscheller, Woertz, et al., 2003; Pfurtscheller, Neuper, Pichler-Zalaudek, et al., 2000) and was shown to provide reliable decoding of the motor termination process. The results show that subjects could maintain good performances by exhibiting β rebound over central channels resulting in higher decoding performances compared to the subjects still relying on the contralateral channels.

The research presented in *Chapter 5* investigated the effect of the breathing process on BMI based on an adapted MI paradigm. The data show that respiration signals affect the correlates of MI (ERD in μ and β bands) as well as the user's actual BMI performance. From this study, three main outcomes can be taken with: i) the finding of an effect of the breathing cycle on the neural MI correlates in the μ band; these were characterized by stronger ERDs during the late expiration phase. I also showed (ii) the possibility to predict BMI performance from the respiration rate because of an indirect effect mediated by the β bandpower and (iii) revealed an effect of the breathing cycle on BMI performance: there was a significant increase of True Positive Rate when BMI is trained on inhalation-locked starting cues showing compared to when it is trained on expiration-locked. In summary, this study shows the importance of monitoring breathing signals and more generally presents the interoceptive system as a key component of motor preparation and motor imagery.

6.2 Future directions

6.2.1 Motor termination and BMI

This thesis contributes to the understanding of the neural mechanisms involved in an hand MI task and notably on its motor state transitions. More, through the different studies, the importance and the benefits to detect such transitions were highlighted in the context of BMIs. Additionally to these studies, some future directions could be envisaged to use this approach for BMIs as well as to have a better understanding of the mechanisms involved in the stopping

process.

Variability of correlates in Motor Imagery - All the experiments were performed with the same BMI paradigm and aim to control and monitor the stopping process in MI. Despite this consistency of framework, significant differences regarding the correlates of motor termination were observed within our experiments (Chapter 2-4). This is likely explained by the instruction given by the operator regarding the type of MI task to perform. Indeed in Chapter 2, subjects were instructed to perform a repetitive MI action while for Chapters 3-4, because the objective was to control an exoskeleton, subjects were instructed to perform a continuous MI action since being closer to the actual movement the exoskeleton would exert on the hand of our subjects. Hence, the type of MI task and task instructions constitute an important parameter for decoding BMI and should be considered as a key factor (Nam et al., 2011; Stancák Jr and Pfurtscheller, 1996), highlighting cognitive contributions to BMI (Evans and Blanke, 2013; Marchesotti et al., 2016). Thus, one could perform an extensive characterization of the correlates of motor termination in the different types of MI used in BMIs.

Longitudinal neurofeedback training - Another challenge of decoding MI termination observed in this thesis was the complete absence of the neural correlates of motor termination (e.g. β rebound) in few subjects. Different studies have indeed reported that not everyone exhibits these correlates (Pfurtscheller et al., 2005). In this previous study, the absence of β rebound was shown more often during hand MI tasks compared to feet MI tasks. Since this thesis was focused on the termination of upper limb movements to promote more natural and intuitive interaction between BMI users and machines, it is not surprising that the absence of β rebound in some subjects was also reported, with such cases occurring even when subjects were presenting correlates of MI. Hence, to reduce this variability, one solution could be through a neurofeedback training to promote or reinforce the correlates of MI termination. This approach was already successfully used in the context of MI-based BMI (Kus et al., 2012; Omura and Kanoh, 2017) and hence could be investigated in order to modulate the β rebound. This method could also be an interesting way to promote specific localization of this rebound such as central channels in the case of BMI users aiming to control a BMI effector (e.g. an exoskeleton).

Combination with other neural correlates in BMI - To increase the reliability of BMIs, researchers often combine different signals by exploiting the different nature of BMI signals. This reasoning could easily be applied to the decoding of MI termination. For instance, the combination with Error Related Potentials (ErrPs) - exogenous response to cognitive stimuli occurring when an error is presented in a system (Schalk et al., 2000) – could be worth investigating. In the past, this signal was often combined with other signals to increase the reliability of BMI (Ferrez and Millán, 2008; Schmidt et al., 2012; Spüler et al., 2012). To the best of our knowledge, such a signal was however not combined in the frame of movement termination. Note that although by default these signals would be only introduced because of erroneous behavior of the BMIs, this last could however be used as a second control to ensure the interruption of the BMIs. Such a combination could also represent a suitable solution for
subjects that do not exhibit correlates of MI termination. More, post-hoc analysis showed the presence of ErrPs in our data during a closed-loop operation with the exoskeleton (Chapter 4). Importantly, the exoskeleton does not seem to affect the ErrP signal (see Fig. 6.1) hence showing promises to be used for this purpose. Interestingly, we can also observe that ErrPs tend to be larger when subjects stop too early (undershoot condition) compared to when stopping too late (overshoot condition). Based on this result, a proposed approach could be to run an asynchronous decoding of ErrPs (Lopes-Dias et al., 2019). In an undershooting scenario, this decoding could invalidate the stopping decision taken by our approach while in an overshooting scenario, this could be used as a second gait for controlling the stopping process of an interface. More details on the methods can be found in Annex 7.1.



Figure 6.1 – Grand-averaged error-related potentials on the FCz channel. Trials were categorized in three different categories based on the latency of the BMI to stop the clock (t=0) with respect to the stopping cue (undershoot: [-inf,0.5] s, correct: [0.5, 1.5] s, over-shoot: [1.5, inf] s). ErrPs for each type of trial (Green: correct, Red: undershoot, purple: overshoot) are shown on the plot. The lines show the average over subjects (N=13) while the dash regions represent the standard error.

Clinical application of decoding motor termination - Beside being used for stroke or spinal cord injury survivors, the presented approach could also be useful for patients suffering from Parkinson's disease. Indeed, it was shown that closed-loop Deep Brain Stimulation (DBS) can affect the returning phase of a reaching movement. This effect is characterized by an increase in the number of sub-movements introducing for the subject a delay for the movement termination (Iturrate et al., 2019). To counter such unwanted effects in these patients, one could decode the motor termination which could help to turn off the stimulation and consequently to suppress the observed delay of movement termination. The proposed approach was tested on offline data recorded on three patients implanted with Deep Brain Stimulation (DBS) while performing a reaching motor task with their most affected hand in three different stimulation conditions: without stimulation (OFF), with continuous stimulation at 130 Hz (ON), and with an adaptive closed-loop stimulation (ADA). Using our approach, the ability to decode movement termination was evaluated and the results were reported below (see Fig. 6.2). The results show decoding accuracies above the chance level; hence demonstrating the feasibility to detect movement termination in Parkinson's patients. Methods



from this piloting study can be found in Annex 7.2.

Figure 6.2 – Classification results on detecting motor termination. **A**. Classification accuracy for each subject (s1, s2, s3) and in grand average (GA) under the three different stimulations (stim OFF: no stimulation, stim ON: continuous stimulation, stim ADA: closed-loop stimulation based on Beta burst detection). The red horizontal line indicates the chance level calculated for each classification and by permutations (N=5000 permutations). Statistical Analysis was also performed and reported on the plot (* p<0.05, ** p<0.01). **B**. Pseudo-online for each subject (S1, S2, S3) and averaged over them (GA) under the three conditions of stimulation. The orange line (time t = 0) indicates the starts of the returning phase.

Here, these results introduce how the decoding of movement termination could be used for clinical applications with the example of switching off DBS stimulation in Parkinson's patients. Importantly, the same approach used to detect motor termination during an imagined movement (MI task) was used for real movement execution. Then, using our approach could help to improve the motor behavior of the patient during a reaching task which could drastically decrease the number of sub-movements enforced by the closed-loop stimulation. The combination between machine learning and stimulation could present clinical improvements to the current therapy and is a good example of how decoding movement termination can be used. Importantly, although these results are encouraging, the use of such an approach for clinical applications would need (1) to be validated on a larger population to fully understand its reliability and (2) to improve the decoding performances by the use of advanced machine learning algorithms which would mainly require larger training datasets.

Overall, the presented approach based on the motor state transitions could allow BMI users to control not only the activation of BMI effectors but also and especially the stopping process involved during upper-limb movements (execution or imaginary). In the context of rehabilitation technologies, this could present a non-negligible advantage for therapist training patients to use BMI. Indeed, one could argue that such an approach could promote more functional movements, and by doing so, may facilitate neuroplasticity leading to a faster recovery. Moreover, this two-way dual control could also represent an alternative to continuous control of devices. As previously mentioned, continuous control represents a major challenge

in the field (Soekadar et al., 2016). In this scenario, BMI users are asked to modulate their MI correlates and map them according to the device operation. For instance in the case of an hand exoskeleton, with the degree of grasping, a user is required to maintain a precise amount of motor intent in order to keep the exoskeleton in a specific position. Hence, continuous control requires from the user a constant attention and effort which cannot be conceivable for daily use. Thus, the decoding of motor state transitions could be also an interesting alternative to continuous control.

6.2.2 Breathing and BMI

In the last part of the thesis, I investigated the effect of breathing signals on the EEG correlates and the BMI performances in MI paradigm. Similarly to Park et al., 2020, our data shows that brain fluctuations during MI task are driven by breathing signals, hence, impacting BMI performances as well. Since this work represents the first attempt to link BMI and the interoceptive system, the following part of this section contains a list of follow-up studies that could be done in order to address in more depth the role of breathing in BMIs.

Breathing effect on correlates of Motor termination - As this study investigated the effect of breathing on MI initiation, it would be interesting to investigate the correlates of MI termination as well. This analysis was however not possible in our previous experiment since these correlates were not exhibited by the majority of our subjects. Indeed, because the transitions were triggered based on the breathing cycle, our protocol needed to differ from the original protocol used in the other chapters (Chapters 2-4). Hence, in this protocol, subjects were not able to foresee the termination of their MI action. This could be one reason why the presence of β rebound or other correlates of motor termination were not observed. Hence, by investigating the effect of breathing on correlates, one could expect to have a coupling as well between the breathing cycle and the power of β rebound which could be characterized by a stronger increase of power in the inspiration phase.

Breathing effect on BMI during closed-loop operation - To fully investigate the effect of breathing signals on BMIs, an important factor that was not addressed in our last study was the evaluation of such effect during a closed-loop scenario. Indeed, it is well known that a strong behavioral difference can be observed between the calibration phase of a BMI and its real-time performances (Chavarriaga et al., 2017). Hence, it is then important to perform a similar analysis in the context of closed-loop scenarios. Particularly, one could analyze the breathing patterns when looking at the timing when the decision was made by the BMI. In this regard, we started a pilot study with up to now 14 subjects recruited. Preliminary results tend to show a similar effect on the correlates of MI (see Fig. 6.3) with a stronger desynchronization in μ band (μ -ERDs) during the late expiration phase (non-parametric permutation test on modulation index, p = 0.041 < 0.05, N = 1000 permutations). Hence this result confirms so far, the previous analysis done in Chapter 5. Moreover, these preliminary data suggest that the decision itself of the BMI is also influenced by the breathing cycle, further proving solid



Figure 6.3 – Respiratory phase coupling analysis for μ power activities in self-paced trials. ERD/S power was calculated for each channel for the 6 equally sized bins of the respiratory phase (x-axis). From the band power, a topographic map was represented for the μ and β band power activities at the decision time of the BMI. The average band power of the contralateral EEG channels (C3, CP3) and was calculated for each subject (time point). The mean over subjects was reported on the figure (blue color) with the horizontal line representing the standard error.

evidence of how breathing impacts BMI control. More details on the experimental design can be found in Annex 7.3.

In this pilot study, the evaluation of how well the BMI decision corresponded to the correct motor intent was assessed based on the rate of the agency i.e. the sense that it is them or someone else causing or controlling the movement of a virtual hand (Gallagher, 2012). Hence another interesting question would be to understand if this sense of agency could be affected as well by the breathing cycle. However, no significant link between the agency and the breathing was found so far in our data. This result is likely explained in reason of the high variability within our subjects basing their rate on different factors leading to a subjective and unreliable rating. Hence clarity and carefulness should be very important when explaining this rating system to the subject.

6.3 Conclusion

In conclusion, this thesis proposed a novel approach for the design of EEG-BMIs based on motor state transitions with the main focus on the stopping process occurring during movement imagination. Such an approach holds great promise to be used in the context of upper limb movements and could enable users to unlock finer control of their BMIs while promoting more natural and intuitive interactions. To use this approach, the effect of breathing signals should be also closely monitored since as we pointed out in this thesis, the breathing system has an intrinsic role in the correct functioning of BMIs. Hence, to use our approach and more generally BMIs, it is primordial to promote or reestablish the correct functioning of the interoceptive systems as a primary step.

7 Annexes

7.1 Analysis of Error Related potentials in closed-loop operation

7.1.1 Online Protocol

After performing the offline protocol described in Chapter 4, 13 subjects performed the same protocol in closed-loop operation while still having the exoskeleton inducing a passive movement on their right hand. Here, those participants were actively controlling a clock using their MI action and through the use of a finite state model with the sequential use of two decoders. Both decoders were trained on the offline data (see Chapter 3) to respectively detect the onset and the offset transition of MI action. Participants' task was first to initiate the clock hand and to stop when the clock crosses the target based on their MI action. Each subject performed 4 runs of 15 trials each (60 trials in total). Contrary to the offline protocol, the gauge was changing based on the BMI output of the onset decoder as a source of continuous feedback. This continuous feedback was present only for MI onset detection. Here, BMI output corresponded to the integration of the output probabilities of the decoder to each single EEG sample based on an exponential moving average. The smoothing parameter α was set by the operator and kept fixed for the rest of the experiment.

Accordingly to the finite state model, once the onset transition was detected, a second decoder was launched and focused on the detection of the MI termination. Here, only discrete feedback was provided to the user (i.e. the clock stopped once MIt was detected). The detection of MIt was based on an accumulated decision, i.e. counting the number of times the decoder was detecting MIt (p(t) > 0.5). This parameter was set by the operator and kept fixed for the rest of the experiment as well.

7.1.2 ErrP Analysis

During this online protocol, EEG signals were recorded at a sampling frequency of 512 Hz with 16 active surface electrodes placed over the sensorimotor cortex i.e., on positions Fz, FC3, FC1,

FCz, FC2, FC4, C3, C1, Cz, C2, C4, CP3, CP1, CPz, CP2, and CP4 according to the international 10/10 system (reference: left earlobe; ground: AFz; gtec gUSBamp, Guger Technologies OG, Graz, Austria). The amplifier was set with a hardware band-pass filter between 0.01 and 100 Hz (Butterworth 4th order) and a notch filter between 48 Hz and 52 Hz. A common average reference was used on the EEG raw data to enhance the signal-to-noise ratio. In a post-hoc analysis, EEG signals were bandpass filtered at [1, 12] Hz with a causal 4th order of Butterworth filter. A spatial filter was then applied using Common Average Reference (CAR). The trials were split into the three different categories and based on the latency between the offset cue and the actual stop detected by the BMI cue (undershoot: [-inf,0.5] s, correct: [0.5, 1.5] s, overshoot: [1.5, inf] s). The average amplitude on FCz channel was then plotted for each condition in Fig. 6.1 (see Chapter 6).

7.2 Decoding of movement termination during DBS in Parkinson patient

The present annex contains materials from the following article: Iñaki Iturrate, Stephanie Martin, Ricardo Chavarriaga, Bastien Orset, Robert Leeb, Aleksander Sobolewski, Etienne Pralong, Mayte Castro-Jiménez, David Benninger, Jocelyne Bloch, José del R. Millán; "Beta-driven closed-loop deep brain stimulation can compromise human motor behavior in Parkinson's Disease"; bioRxiv 696385; July 9th, 2019.

7.2.1 Protocol

After STN DBS bilateral implantation (36 to 48 hours), three patients were asked to perform a reaching motor task with their most affected hand. Patients were placed in front of a touchsensitive screen. They were first instructed to press a button placed in front of them (resting condition). This was followed by the appearance of a circular target with a randomized position on the screen. Patients were asked to reach and touch the target with the index finger as fast and accurately as possible. If the patients were pressing inside the cue area, the cue would turn green while turning red if outside. After that, patients were returning to the resting position on the button (see Fig. 7.2). Importantly, the task was performed under three different stimulation conditions: without stimulation (OFF), with continuous stimulation at 130 Hz (ON), and with an adaptive closed-loop stimulation (ADA). The stimulation took place unilaterally in the hemisphere contralateral to the most affected upper limb. During closed-loop conditions, the stimulation was triggered based on the β burst detection. To do this, a threshold was found during a resting-state period of six minutes before the experiment. This threshold was decided based on the 50th-percentile of the smoothed β power. Due to different physical conditions, the number of trials was varying between subjects and conditions between 30 to 58 trials. The hand kinematics was also recorded using a 3-axis wireless accelerometer placed on the subject's wrist (Shimmer sensing, sampling rate 50 Hz).



Figure 7.1 – Experimental Protocol. Patients were instructed to perform a reaching task where they rested their most affected hand on a button while facing a tactile screen. When a cue appeared, patients had to reach and press the cue as fast and precisely as possible and come back to the resting position. The reaction, reach and return times, spatial inaccuracy, and acceleration profiles were measured. The figure was taken from (Iturrate et al., 2019).

7.2.2 Offline Classification

Using only the temporal amplitude of the β band from both areas (left and right hemisphere), we trained a decoder to detect the termination of a movement while the presence of the adaptive stimulation. Features were extracted within a 0.5s window, yielding a total of 512 features. A 5-fold trial-based cross-validation was performed where the 10 best features from each fold were selected based on their Fisher Score. Using these features, a Diagonal Linear Discriminant Analysis (DLDA) was trained. Feature vectors were extracted from each sample in the training dataset and z-score normalized. Their mean and variance were applied to the feature vectors in the testing dataset. The movement termination decoders were trained to distinguish between sustained movement and movement termination. 0.25-second-long samples were computed with a sliding window (shifted every 12.5 ms) in the time intervals [-0.7, 0] s (reaching phase) and [0, 0.7] s (returning phase) with respect to the time when the patients were touching the screen (t=0). To assess the classification performance, we calculated the accuracy at the sample level over the 5-fold cross-validation. The accuracy was defined as the number of correctly classified samples over the total number of samples and was computed

for each fold. For each subject, we estimated the chance level by permuting the labels 5000 times. Additionally, we performed a pseudo-online analysis to estimate the behavior of our decoding approach in a simulated real-time scenario within the cross-validation process. To do this, we create a buffer that we shift every time samples. We applied our decoder to this buffer and recorded the decoding likelihood of movement termination. The results were then averaged over trials and folds.

7.3 Evaluation of breathing effect on BMI in closed-loop operation

7.3.1 Protocol

A total of 14 healthy naive subjects (6 women, right-hand dominant) participated up to now in this piloting study. All participants were compensated for their participation and provided informed written consent in accordance with the Cantonal Committee of Vaud, Switzerland for ethics in human research (CER-VD). Subjects were first trained to control a classical BMI. In this training, subjects were instructed to perform a kinesthetic Motor Imagery (KMI) task of their right hand, i.e. imagining the feeling associated when they squeeze their hand. Subjects were performing either MI action or a resting-state within three runs of 30 trials with a 1:1 ratio (MI: REST). Subjects were placed in front of a screen and instructed to constantly look at a fixation cross placed in the middle of the screen. For each trial, a filling gage (from the center toward one of the cross extremities, left for REST and right for MI) indicated a 5-s duration to perform either MI or REST. After the calibration phase, subjects were testing their BMI in a closed-loop operation (20 trials). Similarly, as before, subjects were asked to perform MI action or resting-state, this time the filling gage was corresponding to their decoding likelihood to perform MI. Their decoding likelihood was passed through an evidence accumulation module (Perdikis et al., 2011) to smooth the probabilities for visual feedback. Importantly, during this testing phase, a threshold for MI was set for each subject, the alpha parameter from the evidence accumulation module was slightly changed if needed as well but kept constant all the rest of the experiment.

After calibration of the BMI decoder, a second experiment could start and was performed in a closed-loop scenario. Subjects were placed in front of two virtual hands with only the right virtual hand-animated (i.e. closing hand animation). During 5 runs of 60 trials, subjects were asked to activate the hand using their MI action (see Fig. 4.1). At the end of each trial, the subject was instructed to rate his sense of agency with respect to the time the decision was made (from 1 to 9). In this experiment, two conditions were presented to the subject. Importantly, both conditions were randomized within each run (40 cued trials, 20 self-paced trials). In the cued condition, the user was asked to start as soon as the GO signal was shown, independently of the subject will and without him knowing it, the hand was automatically animated after a certain time varying between 1 to 3s (calibrated for each user based on the time to activate their BMI). In the self-paced condition, the user was asked to initiate his MI action whenever he wanted within the trial, the hand was animated only once the BMI was reaching a decision. In total, 100 trials were performed in the self-paced condition while 200 trials in the cued conditions.



Figure 7.2 – Protocol design for piloting experiment. During the experiment, EEG was acquired through 64 electrodes ANTneuro eegoSports system. In the experiment, two types of trials were randomized within each run (cued trials and self-paced trials). For cued trials, a Go signal was given between [1, 2.5] s after the trial started. After a random delay ([1.5, 3] s, the hand closing animation was launched, Visual Feedback). For self-paced trials, the subject was instructed to start his MI action whenever he wanted. Using the last 1s-sample, a decoder was output the likelihood to detect MI. Once a certain threshold was reached, the hand closing animation was delivered. In both conditions and at the end of each trial, the subject was asked to rate his sense of agency from 1 to 9.

7.3.2 Classifier Training and Analysis

EEG signals were recorded at a sampling frequency of 512Hz with 64 active surface electrodes according to the international 10/10 system (reference: CPz; ground: AFz; AntNeuro eegoSports system). Power spectral densities (PSD) were computed in a 1s-window based on Thomson's multitaper power spectral density (PSD) estimation from 8 to 30 Hz with a 1 Hz resolution on selected channels (FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4, CP3, CP1, CP2, and CP4), yielding a total of 308 features. All the training samples were used to train a random Forest algorithm (n= 1000 trees, max depth = 5) to distinguish between MI and resting-state. For MI and resting-state tasks, a 1s-window was shifted every 62.5ms between the intervals [0.5, 4.5] s to augment the number of samples per trial. The same analysis performed in

Chapter 5 was then performed at the time of the BMI decision and reported in Fig. 6.3 (see Chapter 6).

7.3.3 Respiration Phase

Respiration data were band-pass filtered between [0.01, 10] Hz. The respiratory phase was calculated by applying a Hilbert transform and taking the angle of the complex argument. For the phase coupling analysis, the respiratory phase was binned into six equally sized bins.

7.3.4 Phase coupling Analysis

A spectral analysis was performed to compute the event-related spectral perturbations (ERSP). In this analysis, the power was calculated with the following equation and averaged over subjects:

$$ERD/ERS = 10 * log(\frac{A}{B})$$
(7.1)

Where A represents the power activity for a frequency of interest at a given time and B represents the average power during a baseline interval, chosen between [-2, 0] with respect to the starting cue.

The average power was calculated over μ band ([8-12] Hz) the contralateral channels (FC3, C3, CP3) corresponding to the electrodes of interest for MI tasks. The data were then epoched and the z-scores normalized over the trials. We extracted the power at the time (t=0) corresponding to the time when the BMI detected MI.

From each trial, the respiratory phase was extracted at that time. The power from all trials with the same respiratory phase was then grouped in the same bin. Additionally, a topographic map was plotted for the μ band with respect to the binned respiratory phase.

7.3.5 Permutation test

For each subject, the band power for each bin and trial was randomly permuted (N=1000). For each permutation, the modulation index was calculated. This modulation index is a measure that quantifies the deviation of a defined amplitude distribution from a uniform distribution (Jiang et al., 2015). Based on the 1000 permutations, a distribution of the modulation index was found and averaged over subjects. This distribution was compared with the real grand average modulation index. A p-value was calculated from this comparison.

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About me –

- Biomedical Engineer
- Data Analysis/Machine Learning
- Brain-Machine Interfaces

Skills -



Languages

French (Native)

English

Italian

(*)[The scale is from 0 (Fundamental Awareness) to 6 (Expert).]

Experience

2017-2021	 Applied Machine Learning Engineer [PhD thesis] Laboratory of Cognitive Neuroscience (LNCO) Defitech in Chair in Non-invasive Brain Machine interface (CNB) Detection and Classification of movement using brain signa Feature Engineering in time and frequency domains. Real-time control implementation (e.g. exoskeleton, wheelc Applied statistical models (e.g. regression, GLM). 	FCBG [) ls hair).
2017-2019	 Machine Learning Teaching assistant Teaching Master Courses at EPFL (School of Electrical Engineer Data Analysis and Model Classification Brain Computer Interaction 	EPFL ring)
2016	 Junior Data scientist [Master Thesis] Nicolelis lab, Duke University medical center Classification and Feature engineering on neural dataset. Pipeline for neural data preprocessing with Unit Testing Development of paradigm with rhesus monkeys(C++) 	DUKE
2014	 Pipeline Automation Engineer Laboratory of research in Neuroimaging (LREN) Automatization of an MRI pipeline analysis(Matlab) Data Compression with Bash scripting Development of a SOL-based database for patient recruiter 	синv

Education

2017-2021	Ph.D. in Neuro-engineering Funded by National Centre of Competence in Research (robotics	EPFL (NCCR) in
2014-2016	M.Sc. in Neuroscience and Neuroengineering	EPFL
2010-2014	B.Sc. in Life Sciences	EPFL

Certificates

2020	Tensorflow Professional Developper Certificate Coursera - DeepLearning.ai
2020	Deep Learning Specialization Coursera - DeepLearning.ai

Extra curricular

Active member in HackaHealth

<u>HackaHealth</u> is an association organizing hackathons aiming at engineering personalized solutions for people with motor disabilities to improve their daily living

[Project] Assistive tool to use keyboard for stroke patient

Hand2keyPressedRehab provides a solution to send keys pressed using hand gestures detection (Leap-motion) for person with motor disabilities

• [Project] Hand Tracking for mouse control

HandTracking translate the movement of the hand to control the mouse through Computer Vision (HSV Filter, HandPose estimation)