BCI-Based Facilitation of Cortical Activity Associated to Gait Onset After Single Event Multi-level Surgery in Cerebral Palsy

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Abstract Motor rehabilitation strategies by means of neuro-modulation paradigms, taking advantage of the motor predictive characteristics of the electroencephalographic signal, are currently subject to extensive research. Such rehabilitation strategies follow a top-down approach in which targeted neurophysiological changes in the central nervous system are expected to induce functional improvement. However, such approach presents a set of specific limitations and barriers in cerebral palsy patients, given that they typically do not have a normal gait and have suffered abnormal brain development. These limitations get even more critical when Single-Event Multilevel Surgery (SEMLS) is performed. After that procedure, surgery patients must re-learn the gait patterns according to a new biomechanical structure. This chapter presents a neuro-modulation paradigm to enhance the reeducation of gait functionality immediately following SEMLS in cerebral palsy patients. The experiments were developed and tested with real patients.

Keywords Neuromodulation · Virtual reality · Cerebral palsy · Gait neurorehabilitation · Single-event multilevel surgery

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1 Introduction

Cerebral palsy (CP) is a disorder of posture and movement due to a defect or lesion in the immature brain. It is estimated that 17 million people worldwide are affected [1]. In many cases, the development of secondary musculoskeletal pathology contributes to loss of function, gait impairments, fatigue, activity limitations, and participation restriction. In fact, one out of three CP patients is unable to walk. For those patients, orthopaedic surgery is considered one of the best treatments for significant musculoskeletal problems, and thereby minimizing the subsequent impairments and activity limitations. One of the main techniques is multilevel orthopaedic surgery, which focuses on correcting all deformities and to improve gait. It is often referred to as Single-Event Multilevel Surgery (SEMLS) when is performed in a patient without previous surgeries. SEMLS refers to the procedure encompassing several orthopaedic surgeries in one intervention, affecting two or more levels of the lower limbs (knee and ankle, for instance). It differs from other multilevel approaches in that SEMLS is based on the biomechanical principles previously obtained by 3D gait analysis [2]. Currently, SEMLS is indicated up to 70% of CP children under 14 years old. SEMLS has shown benefits in the treatment of musculoskeletal problems of children with CP by reducing the effort and the appearance of walking, improving Gross Motor Function Measure (GMFM) [3], kinematic parameters, gait speed, and Gillette Gait Index score [4]. After this procedure, a period up to 2 years is often required to get a functional plateau level, although there is a lack of published recommendations about the more efficient post-surgical rehabilitation program. New strategies are needed to help to promote, maintain, and rehabilitate the functional capacity, and thereby diminish the dedication and assistance required and the economic demands that this condition represents for the patient, caregivers and society.

Most therapies for rehabilitation after surgery are peripherally driven and are based on motor control reorganization triggered by peripheral physical therapy. However, CP affects primarily brain structures. This suggests that both the Peripheral Nervous System (PNS) and the Central Nervous System (CNS) should to be integrated in a physical and cognitive rehabilitation therapy. This is exactly the approach proposed in this chapter. It is important to highlight the plasticity of the target patients of this study: young children present increased brain plasticity compared to an adult, and are more likely to exhibit a change in motor patterns following an intervention.

Consequently, a BCI system is proposed here in two phases: the first one as re-education of gait-related cortical activity (post-surgery intervention in bed or wheelchair); the second one as active control of the rehabilitation therapy on the robotic platform. Therefore, the first month post-surgery, when the patient is immobilized, is the most appropriate period to prepare the brain for the new gait patterns later promoted with the robotic physical rehabilitation process.

2 Neuro-Modulation in Cerebral Palsy Patients—BCI Perspective

One possible application of BCI that has garnered significant research interest during the last decade is its use to restore motor function by inducing activity-dependent brain plasticity for brain motor re-learning [5]. According to this approach, known as top-down [6], BCIs use brain activity to promote central motor control by operating on the peripheral nervous system in order to recover motor function for people with severe motor disabilities. The objective of these BCI therapeutic applications differs from the BCI applications for communication and device control, since the former application attempts to maximize motor planning ability damaged by disease or trauma by performing tasks related to motor execution or motor imagery.

In any case, there is scarce scientific work about the potential use of BCIs by CP patients independent of the type of application and objective. The complexity associated with the experimental design, given the great amount of symptoms that vary from patient to patient as a consequence of the different brain areas affected, necessitates analysing and meeting individual specific conditions and requirements to identify brain activity evoked by external stimuli or subject to the patient's control. Therefore, the existent works are rather exploratory studies that intend to lay the foundations for developing potential uses of BCI in CP individuals.

In [7], a case study to train a severe paralyzed CP patient by an EEG-based BCI for verbal communication is presented. The patient could produce two distinct EEG patterns by controlling frequency features of sensorimotor rhythms during movement imagery.

The proposal for using ECoG techniques to record brain signals in speech cortex shows an efficient way, with a good spatial and signal-to-noise resolution, to build BCIs for spastic CP patients presenting the motor cortex damaged [8]. The resulting processed signal, representing the intent of the patient, could control different types of computerized devices, including rehabilitation systems. Both studies belong to the BCI paradigm for communication or device control.

A well-known work dealing with a larger population of CP patients, to investigate their ability to gain control of two online BCIs that assist them with their communication needs, is described in [9]. Fourteen individuals with different types of CP were engaged in this experiment by using two different electroencephalographic phenomena, one based on endogenous sensorimotor rhythms (SMR) and the other one based on potentials evoked by exogenous visual stimuli (SSVEP). Both BCIs involve different cognitive processes and cortical areas. SSVEP-based BCI involves attending to oscillatory stimuli that increases in magnitude the activity recorded in the occipital cortex at the corresponding frequency. SMR-based BCI implies carrying out different mental tasks as mental arithmetic or motor imagery of some part of the body. The results of this work show that not all approaches work for every user, although the SMR-based BCI is better commanded by a larger number of users, and that there is no statistical relation between degree of impairment and the ability to control a BCI.

In healthy people, SMR-based BCIs implicate motor cortex areas that exhibit rhythms whose amplitudes typically change with the movement, the stimulation or sensation and also during motor imagery [10]. Since these rhythms are associated with cortical areas most directly connected to the brain's normal motor output channels, they could be a potential tool for BCI neuro-rehabilitation.

However, the possible motor-cortical lesions in CP patients can alter the neural mechanisms underpinning actual motor execution and motor imagery. In an EEG-based brain mapping study [11], with four healthy children and four children with CP, children with CP showed asymmetrical and global topographical maps regarding SMR rhythms changes when they perform motor imagery tasks compared to healthy children. Another study [12] also focuses on understanding the neural processing underlying BCI control using motor imagery in fourteen CP individuals and twelve healthy individuals, and found significantly lower SMR modulation and connectivity strengths between cerebral areas in CP patients. Although motor imagery training seems to be a promising method to improve motor control in CP, its efficacy needs to be proved by empirical testing.

Summarizing, building a BCI for neuro-rehabilitation purposes in CP patients requires analysing and determining cortical activity and brain areas with neuroplastic potential in a tailored manner, given the congenital damage in their brains. This damage impairs motor planning ability that affects motor execution and motor imagery tasks. Another key aspect to assess lies in the nature of the motor imagery tasks to be proposed, since this population presents impaired sensorimotor integration leading to decreased body awareness. So, promoting body awareness in CP patients when they perform motor imagery tasks by a suited experimental design and paradigm is critical to produce a kinaesthetic image of the motor action and to obtain viable electrophysiological activity. Other crucial issues to take into account are the familiarity of the motor tasks and the imagery instructions in order to encourage the motor imagery capacity in CP.

3 Particular Drawbacks for BCI-Based Motor Neuro-Rehabilitation in Cerebral Palsy Patients Following SEMLS

Due to the very early brain damage and functional limitations, CP patients exhibit abnormal brain development [13]. This causes abnormal brain activity that in turn hinders the decoding of useful information from that activity. In order for a BCI to be effective in motor rehabilitation, motor-related activity should be potentiated by a coherent proprioceptive feedback. Given that BCIs should be non-invasive and easy to wear for the sake of applicability, the most suitable way of measuring the brain activity is Electroencephalography (EEG).

In this sense, there are three main types of disability concerning motor function in CP patients that also alter EEG motor-related brain activity, thus making BCI application more complicated:

- Spasticity. It is the most common dysfunction. It arises from motor cortex damage making muscles appear stiff and tight. Since it implies motor cortex damage, the brain activity in that area is also abnormal and difficult to use for BCI. Besides, the constant muscle activation produces proprioceptive feedback, which is reflexed in activation of somatosensory areas of the cortex that are really close to motor areas. Moreover, the strength of the muscle contraction may cause artefacts that introduce noise in the EEG cortical signals.
- Ataxia. It arises from cerebellar damage. It implies the loss of muscle control, producing shaky movements. It affects balance and sense positioning in space. Although the damage focuses on the cerebellum, the projections to the motor cortex areas also alter the normal cortical activity. Besides, shaky movements and random motor unit discharges represent a complex artefact for EEG-based BCIs.
- Dyskinesia. It arises from basal ganglia damage. It is characterized by involuntary movements. Like in ataxia, damage to the basal ganglia induces abnormal cortical activity through the cortical-striatum loops. The involuntary movements introduce both external and internal artefacts into the EEG motor-related activity.

Apart from the problems introduced by the above mentioned dysfunctions, there are other concerns coming from abnormal development. In terms of the affected limbs, motor pathologies affecting CP patients can be divided into four groups:

- Monoplegia. One limb, either upper or lower, is affected by a motor dysfunction.
- Hemiplegia. This is the most common type, together with diplegia. It affects one side of the body (arm and leg).
- Diplegia. Both legs are affected. The upper limbs may be affected to a lesser extent.
- Quadriplegia. Both upper and lower limbs are affected. The muscles of the trunk, face and mouth are often also affected.

For BCI applicability purposes, monoplegia is the least affecting condition, since the function of the damaged cortical areas is usually assumed by surrounding areas in the motor cortex. However, hemiplegia often implies a cortical reorganization into the contralesional hemisphere [14]. That is, the function of both sides of the body is assumed by the same hemisphere. This makes the decoding of the target side and limb from EEG activity especially hard. This same effect is dramatically augmented in diplegia and quadriplegia, where the reorganization of motor control is unpredictably carried out in other non-motor areas. Consequently, motor function shares cortical areas with a variety of cognitive functions, which in turn makes EEG decoding and neuro-modulation extremely complex.

In addition, CP patients following SEMLS present a particular problem. They have to re-learn walking (either normal or aided), since their structural biomechanics has changed. Given that those patients have never walked before or have not walked normally, their learned brain motor patterns are unusual. Therefore, they are difficult to detect in order to be promoted and guided later on by neuro-modulation to adapt to their new physical capacities.

The difficulty of CP patients for kinaesthetic motor imagery, given their brain damage, abnormal development and poor embodiment, is the ultimate drawback for BCI-based neuro-rehabilitaton. This problem makes the BCI training paradigm hard to accomplish.

4 BCI-Based Gait Rehabilitation for CP Patients Following SEMLS. A Top-Down Approach

The rehabilitation is a therapeutic process that aims to develop the maximum physical, psychological and social potential of the patient [15]. Although 70% of CP patients will manage to partially recover the gait function during development [13], most patients will improve their gait function by SEMLS.

Although the origin of neurologic disabilities is located centrally, conventional therapies have traditionally focused on providing sensory feedback and performing real movements in the affected limbs of the patients. In this sense, they have been based in a bottom-up approach, i.e. the rehabilitation focuses on the peripheral function, which is in turn expected to induce central neurophysiological changes. Nevertheless, the principal mechanisms implicated in the motor recovery of CP patients involve enhanced activity of the motor areas (wherever they were placed) induced by active motor training [16]. While peripheral stimulation has not proven to be a locally specific way of promoting plastic changes, an induced coherent activation of sensory feedback circuits and structures in the primary motor cortex is expected to reinforce cortico-muscular connections according to Hebbian learning principles, and thus support functional recovery [17]. Taking into account that the connection between the sensorimotor cortex and peripheral muscles in CP patients has been altered, such rehabilitation strategy appears to be a logical step to reinforce the cortico-muscular descending pathways to regain gait control.

This implies switching to a top-down rehabilitation strategy, in which the mechanisms that are targeted for modification through rehabilitation are the new central structures of the nervous system in charge of the movement generation. According to this concept, the peripheral rehabilitation is carried out in synchrony with the activity of the functionally associated structures of the brain, or rather triggered by it. The coupling promotes a cause-effect action from intention to execution of movement, thus increasing the associative facilitation of efferent pathways. Indeed, experimental paradigms using Paired Associative Stimulation (PAS, i.e. the application of timely associated electrical stimuli in cortical and muscular regions) have proven to be an effective way to strengthen the cortico-muscular connections [18].

The sensory feedback may induce plasticity underlying the restoration of normal motor control. The basis of these approaches is that activity-dependent CNS plasticity can induce changes at synaptic, neuronal and circuits levels in cortical and subcortical structures of the brain and so produce a more normal motor control [19].

As said before, most CP patients would benefit from SEMLS. However, the ultimate improvement is reached around 36 months after surgery, following an intensive rehabilitation program [20]. Moreover, the improvement is monotonous during that post-surgery period, except the time range between 12 and 18 months after surgery, where there is a monotonous decrease of the Gait Deviation Index (GDI). After that, the improvement resumes [21]. In this sense, the rehabilitation suggests two points for improvement: Increasing the maximum level of functional recovery and reducing the time to reach that maximum by avoiding the recession period in between. For this purpose, the inclusion of the neuro-rehabilitation of motor activity points to a plausible solution. Since CP patients following SEMLS are in bed during the first 3–4 weeks, the neuro-rehabilitation should begin right after surgery to start modulating brain activity before physical gait rehabilitation. Thus, the brain preparation for the novel upcoming biomechanical feelings of patients is hypothesized as a catalyst for a more efficient and effective physiotherapy.

5 A Virtual Reality-Based BCI Intervention for the Neuro-Rehabilitation of Cortical Motor Patterns Related to Gait in CP Patients Following SEMLS

Three CP children, 11, 13 and 15 years old, respectively, were recruited for the study of this novel intervention. They all had a SEMLS operation. All patients presented no cognitive deficit. The children started the first session of the post-surgery BCI intervention few days after surgery. During the all sessions throughout the intervention, the patients were comfortably seated on a reclining pallet with an inclination of 50° (patients were still unable to control their neck muscles). They wore an EEG scalp and virtual reality glasses (Oculus Rift) as shown in Fig. 1.

EEG signals were recorded from AFz, F3, F1, Fz, F2, F4, FC5, FC3, FC1, FCz, FC2, FC4, FC6, C5, C3, C1, Cz, C2, C4, C6, CP5, CP3, CP1, CPz, CP2, CP4, CP6, P3, P1, Pz and P2 (according to the international 10–20 system) using active Ag/AgCl electrodes (Acticap, Brain Products GmbH, Germany). The FCz channel was used as a reference. AFz was used as ground. The signal was amplified (BrainVision actiCHamp, Brain Products GmbH, Germany) and sampled at 250 Hz. The power values (Power Spectral Density, PSD) were estimated in overlapping segments of 1.5 s and for frequencies between 2–30 Hz in steps of

Fig. 1 BCI-based sessions setup during post-surgery immobilization

1 Hz. Welch's method was used to this end (Hamming windows of 1 s, 50% overlapping).

The virtual reality glasses were used to show the patients the experimental environment in first person view. These glasses cover the total of the human vision range, providing an absolutely immersive feeling and, therefore enabling realistic visual feedback able elicit coherent brain activity. This way, the problem of lack of body awareness or difficulty was reduced. The virtual environment consisted of a fantasy world designed with Unreal Development Kit (UDK), an open-source 3D graphic and game engine. It is projected in stereoscopic mode to the glasses for a more realistic experience. Each session corresponds to a walk (in first person) through a defined path around the world. Along the path, there are different obstacles (gates, stones, trees …). Each time the patient gets close to an obstacle, the walk stops. Then the obstacle disappears and the walk slowly resumes. Each obstacle then constitutes a trial. There are 22 different obstacles along each path. In the first two sessions, the walk is automatic, i.e. it is not controlled by the BCI, although the patients are not informed about this issue (sham condition). Patients always though that they were controlling the walk. This is done because the BCI will not likely perform acceptably in the first two sessions, which might disappoint and discourage the children. Therefore, the automatic walks were used as training trials for further BCI control. In the automatic walk, a trial was designed as depicted in Fig. 2.

Patients were instructed to relax when they faced an obstacle and the walk stopped, if they wanted to make it disappear. After that, they were instructed to kinaesthetically imagine they started walking if they wanted to resume the walk. From these automatic sessions, the pair (channel, 1 Hz—frequency band) with the most pronounced and longest average desynchronization (PSD decay) during the

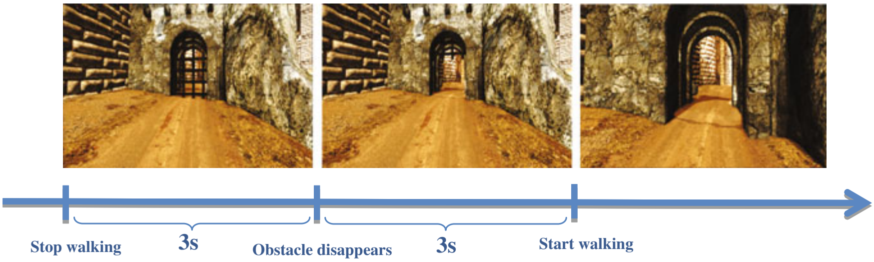

Fig. 2 Description of a trial along the virtual reality automatic sessions

"obstacle disappearing" and "start walking" periods, with respect to the resting periods, was selected. Each session was performed two weeks after the preceding session. Online BCI recording and processing was implemented using BCI2000. A driver was developed to connect BCI2000 and UDK engine.

After the two initial automatic sessions, the best average pairs channel/frequency was extracted for each participant. Given the average time-frequency matrix for each channel, the pair channel/frequency bin with the minimum median value during the 3 s of the obstacle disappearing period, and the first 3 s of the start walking period, was selected. Results for each patient are shown in Fig. 3.

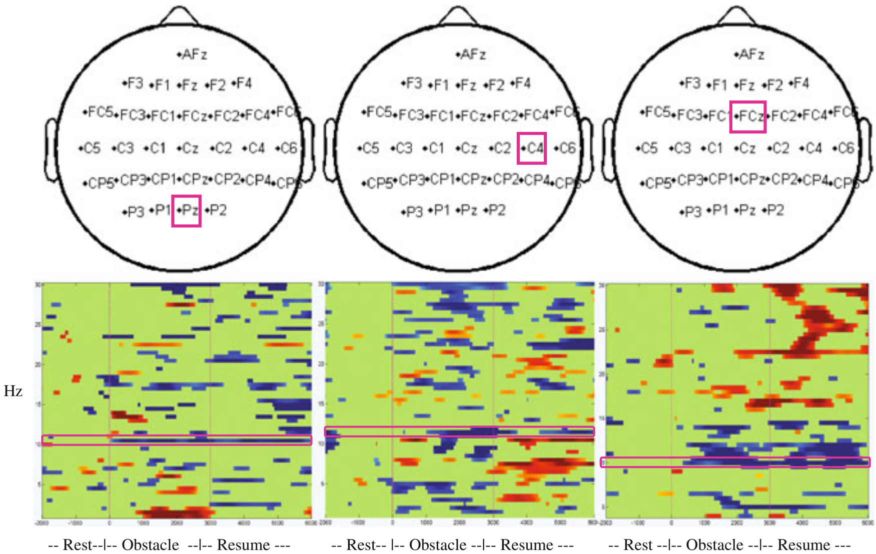

Fig. 3 Average time-frequency graphs showing the most desynchronized pair channel/frequency-bin (*pink box*) during automatic sessions for the three CP patients ($p < 0.05$, with respect to "rest" period; *blue* lower PSD; *red* higher PSD)

The frequency bins selected for gait onset are in the range of *alpha* band or *mu* rhythms (7–12 Hz), the typical frequency of motor preparation. However, the selected channels are diverse and arranges by relevance according to the cortical reorganization described above. Patient 3, with the lowest level of disability, shows a wide desynchronization of *mu* rhythms over the legs area (according to the somatotopic cortical map) of premotor cortex (FCz). However, the two other patients show cortical reorganization of gait onset preparation into other parts of the brain, with a more specialized frequency band.

The patients performed two BCI-controlled sessions along paths different from the automatic sessions. In the BCI-controlled sessions, an obstacle does not disappear until the selected pair (channel, frequency band) reaches the learned power associated with rest and maintains this level for one second (not consecutive) in windows of 2 s. Analogously, once the obstacle disappears, the walk is not re-started until the power value reaches the learned desynchronization for 1 s. The three patients were able to overcome all obstacles and complete the paths.

6 Current State and Future Perspectives

A BCI-based training of cortical activity related to gait has been proposed as a post-SEMLS intervention of CP patients. This intervention prepares the brain during the immobilization period for further physical rehabilitation, thus actively involving the patient in it. The intervention also potentiates the associative facilitation of efferent pathways from cortex to muscles, which in turn benefits the physical rehabilitation. The BCI-guided therapy also boosts the cause-effect feeling of the motor control of the patients, and consequently contributes to increase their sense of agency, in motion terms. Despite the brain damage and heterogeneity, CP patients were able to control the BCI with atypical cortical areas reassigned for gait execution.

Immersive virtual reality has proven to be an effective tool to overcome the problems affecting EEG-based BCI, caused by brain damage, abnormal development, cortical reorganization, new biomechanical structure, impossibility of kinaesthetic imaging of gait and cognitive deficit.

So far, BCI-based neuro-modulation strategies for CP rehabilitation have been able to prove a number of relevant questions in the field. The possibility of developing BCI technology that can be controlled by the cortical waves of patients with cortical lesions has been demonstrated. In addition, recent studies have advanced in the ways to achieve reliable estimations of motor-related cortical states with time precision, which further boosts these neuro-modulation applications. Taken together, these advances represent a strong background for subsequent studies in the near future, in which larger CP populations will need to be recruited in clinical validation studies to further understand the interplay between the BCI reached performance in each person, the attainable neurophysiological changes induced (especially those associated with cortico-muscular facilitation) and the functional improvement of the patients as a result of different rehabilitation intensities with these technologies. To achieve these goals, further developments in EEG acquisition systems and processing algorithms will need to be carried out so that the technology can be easily transferred to the clinical practice. Additionally, further improvement of placebo-controlled conditions must be achieved to fully quantify the relevance of BCI technology in CP rehabilitation.

Finally, the feasibility of using BCI based on residual or new cortical motor rhythms in CP patients opens the door to the application of neuro-robots for gait rehabilitation or re-education [22], which turns out a promising approach [23].

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