

# Exploring the Synergies of a Hybrid BCI – VR Neurorehabilitation System

## Monitoring and Promoting Cortical Reorganization Through Mental and Motor Training

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**Abstract**—Stroke is one of the leading causes of adult disability with a high economical and societal cost. In the last years, novel rehabilitation paradigms have been proposed to make use of the life-long plasticity of the brain to regain motor function. We have developed a hybrid BCI-VR system that explores the idea of combining a personalized motor training in a VR environment - exploiting brain mechanisms for action execution and observation - and a neuro-feedback paradigm – using mental imagery – as a way to engage secondary or indirect pathways to access undamaged cortico-spinal tracks. Here we present the development and validation experiments of the system. The EEG data on 9 naïve healthy subjects shows that a simultaneous motor action and motor imagery paradigm is more effective in engaging cortical motor networks to a larger extent. In addition, we have tested and validated a motor imagery driven BCI-VR version of our system with 9 additional healthy subjects. The results show that users are capable of controlling a virtual avatar in a motor training task that dynamically adjusts its difficulty to the capabilities of the user. User self-report questionnaires indicate enjoyment and acceptance of the proposed system.

**Keywords**—BCI; neuro-feedback; mirror neurons; Virtual Reality; motor imagery; personalization; neurorehabilitation

### I. INTRODUCTION

With about 16 million new strokes per year [1-2], the increasing burden of disease caused by its economical and psycho-social impact makes it necessary to find new diagnostics for preventive actions, more effective treatments to minimize its sequels, and novel strategies for effective, low cost and personalized rehabilitation.

In the last decades, important neuroscientific findings have contributed to the understanding of specific brain mechanisms that relate to functional recovery. Nowadays it is widely accepted that recovery after a stroke relies on neuronal mechanisms that allow non-affected brain areas to take over functions of the damaged tissue [3-4]. This is achieved by means of neuronal plasticity, and the recovery

possibilities strongly depend on the size, severity and location of the lesion [5-6]. Rehabilitation approaches aim at providing an effective way of driving cortical plasticity and recruiting secondary motor areas to achieve functional brain reorganization [7-9]. Recently, the discovery of cognitive processes that mediate between perception and action, such as the Mirror Neuron System [10], allowed the emergence of novel rehabilitation techniques targeting specifically lesions of the central nervous system, such as Traumatic Brain Injuries (TBI) or strokes [11-14]. The use of novel information and communication technologies has played a crucial role in this process. It is by means of technology that neurorehabilitation systems can be tailored to directly tackle the brain mechanisms for recovery. Some examples for motor rehabilitation are robotic-aiding systems [14], Virtual Reality (VR) [7, 12, 14-16] or Brain Computer Interfaces (BCI) [17-19] (see [12] for a detailed review). Given that these novel neurorehabilitation techniques aim at directly mobilizing the above-mentioned mechanisms for functional recovery, they are leading to new breakthroughs in therapy techniques after a neural lesion.

VR is a particularly enabling technology. VR allows creating fully controlled environments that define training tasks specifically designed to target the individual needs of the patients. In addition, thanks to VR, intensive movement training can be embedded in motivating tasks, making use of augmented feedback and reward (see [20] for a review). Besides, VR not only allows for the individualization of training, but it also enables patients to play a more active role in their rehabilitation process, being able to self-monitor their own improvements. Despite all added benefits of using VR in neurorehabilitation systems, the specific characteristics of these systems that make them successful are not yet clearly understood [20]. In our approach, we propose a system that addresses aspects of accessibility, monitoring and a neuro-feedback paradigm.

Accessibility is normally a common limitation. Most of the existing systems are only adequate for a limited number

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of patients that share some specific deficits and generally require a minimum motor control. This situation makes the evaluation of the benefits of these novel technologies in patients that are nearly or completely immobilized particularly difficult. BCI technology has already been used to enable immobilized patients to act and interact with the world [21-22], solving to some extent the accessibility problem. However, fewer investigations have been carried out to make use of this technology to facilitate the access of patients to rehabilitation practices [23-24].

In addition to the accessibility problem, there is the need of more quantitative and comparative data on the effectiveness of interventions in functional terms and the subsequent brain reorganization. This knowledge is essential to be able to prescribe the most appropriate intervention depending on the specifics of each lesion and its prognostic [25-26]. Therefore, it becomes crucial to be able to monitor both functional recovery and plastic changes in the brain simultaneously during as the treatment progresses.

Finally, although neurorehabilitation approaches aim at engaging remaining brain circuits and mechanisms for recovery, most of them do it peripherally by providing “appropriate” sensory-motor input and contingencies [11, 13-14, 27-28]. However, it is generally not well understood what the actual effects are in functional reorganization since imaging data are not always available. Using as principle that synchronized neural activity is an effective way to drive neural plasticity in the Hebbian sense [29], we propose that the more motor-related systems we are able to engage in our neurorehabilitation task, the more likely that secondary or indirect pathways can be recruited and exploited to access undamaged cortico-spinal track fibers for motor control [7, 26, 30]. Therefore, if we were able of monitoring the brain activity, we could use this information in a neuro-feedback paradigm to drive cortical reorganization in a more efficient manner [23, 31-34].

To face the above-described limitations in accessibility, and to provide monitoring and neuro-feedback capabilities, we have developed a novel hybrid BCI-VR neurorehabilitation system. Based on the RGS system, our BCI enabled system provides the right visual stimulation to engage motor areas through the Mirror Neuron System (MNS) [27]. The BCI component is then used to read out activity of motor related brain areas and use it in a neuro-feedback paradigm. Our system enables severe TBI and stroke patients with null mobility to train and potentiate functional cortical reorganization by means of motor imagery. At the same time, patients with some degree of motor control can use the system by exploiting a dual motor and neuro-feedback training paradigm.

## II. METHODS

Our setup consists of a desktop computer, which runs the VR environment, on a tabletop of about 1.4 x 1m. The tabletop is used to support the arms of the users, and arm movements are limited to the tabletop surface. A laptop computer implements the BCI – acquires and processes in

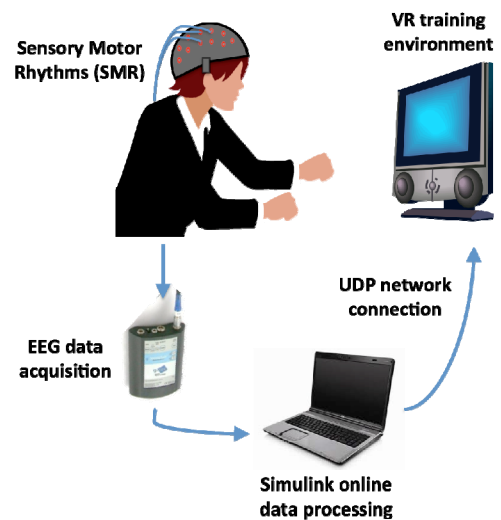


Figure 1. System components and control loop. The EEG data is acquired by means of surface scalp electrodes connected to a biosignal amplifier. Simulink (MathWorks Inc., Natick, MA, USA) is used to log and process the EEG data. Cortical Sensory Motor Rhythms (SMRs) are detected and classified, converting them to control signals for the VR system. The data, sent over a UDP network connection, is interpreted by the VR environment as motor actions of a virtual avatar. See text for further information.

real-time the EEG data from the user – and sends control signals to the VR system (Figure 1).

### A. Virtual Reality

The VR setup is based on the Rehabilitation Gaming System (RGS), a first person perspective VR system that combines concepts of goal oriented action execution and observation with task oriented learning and model based individualization of training to specifically address the recovery of upper extremity functionality after stroke [27]. The RGS brings together VR and neuroscience based rationales exploiting action execution and observation, motor learning, and task-specific individualized training. The main underlying hypothesis is that through the recruitment of the MNS, the combined action observation and execution can activate the motor system more effectively or extensively, and thus enhancing or speeding up cortical reorganization by means of plastic changes after a lesion in the brain. See [27] for a detailed description of the design principles of RGS.

The training task implemented, called “Spheroids”, is a game like task in which the user has to intercept incoming spheres by moving the arms of the virtual avatar. The parameters that define the difficulty of the task (speed of spheres, sphere distance from arm resting position and interval between spheres) are computed at the start of the game in a calibration task (Figure 2, top panel). During this stage of the game, the user is asked to move the virtual arms to specific numbered locations on a virtual tabletop. Arm movement speed, reaction times and movement range are computed from this calibration and used to set the starting parameters of the “Spheroids” training task. The game parameters during training are established by an intelligent controller that online adapts the difficulty to be neither too

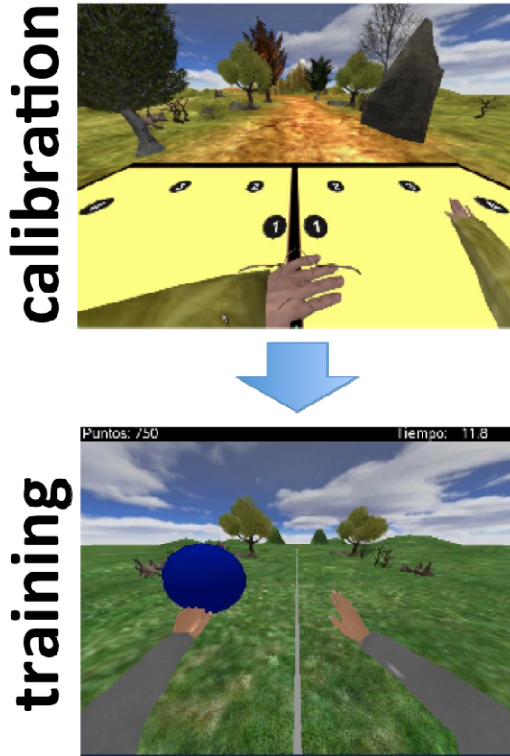


Figure 2. The RGS “Spheroids” training game consists of two phases: a calibration and a training phase. The calibration phase is used to compute the speed, latency and range of the movements of the avatar when reaching for specific locations marked on a virtual tabletop (numbered positions).

The parameters computed in the calibration phase are used to set the starting difficulty parameters of the training phase. During training, the user is asked to control the arms of the avatar and intercept incoming spheres. See [27] for a detailed description of the RGS.

easy nor too difficult, to sustain motivation and to individualize the training to the patient’s capabilities. In addition, the system provides extra feedback to the user to monitor his/her progress in the form of points during the game and performance summaries at the end of the training session (See [27] for a detailed description on the basic RGS setup).

## B. Brain Computer Interface

It is well established that motor intend or motor imagery generates an activation of cortical motor areas consistent with those engaged during the execution of motor actions [35]. The neural activity engaged in these tasks generates electric waves that can be measured from sensors located at the surface of the scalp (EEG). Thus, our BCI component should be able to measure from the primary and secondary motor areas, and map the activity patterns onto movements of the virtual arms to perform the training task in the VR environment.

### 1) Data acquisition and analysis

The EEG raw data is acquired by means of a g.USBamp biosignal amplifier (gtec, Graz, Austria) connected to Au-gold surface electrodes with a 1.5 mm medical safety connector. The g.USBamp amplifier has 16 ADC channels, with a 24 bit resolution ( $<30$  nV) and an update frequency of 256 Hz. The biosignal amplifier was connected via USB to a laptop running Simulink 2007a (MathWorks Inc., Natick, MA, USA). Gtec’s g.Hisys (simulink high-speed online processing library) was used for recording and online processing the EEG data, and g.BSAnalyze (Biosignal analysis library) was used for the classification of Sensory Motor Rhythms (SMRs) in either right or left arm movement (gtec, Graz, Austria). Matlab 2007a (MathWorks Inc., Natick, MA, USA) was used for the offline data analysis.

We used caps with predefined electrode placement locations based on the standardized international 10/20 system to allow for precise and reproducible electrode placement when measuring [36]. In the two evaluation experiments presented in this paper we have employed two different electrode configurations. The first one used a larger amount of electrodes over the sensory motor areas for a more complete assessment during task performance (further referred as *mapping* configuration). The second one used fewer electrodes – easier and faster to set up – for the online classification of SMRs (further referred as *classification* configuration).

The *mapping* configuration consisted of 9 electrodes located at positions  $F_3$  (frontal left),  $C_3$  (central left),  $P_3$  (parietal left),  $T_3$  (temporal left),  $F_4$  (frontal right),  $C_4$  (central right),  $P_4$  (parietal right),  $T_4$  (temporal right) and  $C_z$  (central). From these electrodes, the raw data was filtered into different frequency bands, namely  $\alpha$  (8-12 Hz) /  $\mu$  (8 – 13) Hz,  $\beta$  (12-30 Hz) and  $\gamma$  (30-100 Hz). Each of the 3 frequency bands was logged separately for each of the 9 channels.

The *classification* configuration used only 5 electrodes. Electrodes at  $FC_3$  (frontal-central left) and  $FC_4$  (frontal-central right), and  $CP_3$  (central-parietal left) and  $CP_4$  (central-parietal right) were bipolar derivations (measuring voltage differences between them). The fifth electrode, located at  $FP_z$  (frontal-parietal region), was used as ground. In this configuration, only the  $\alpha$  and lower  $\beta$  frequency bands of the EEG data were considered to detect the SMRs.

In both configurations, a sensor in  $A_2$  (right ear lobe) was used as reference.

### 2) SMR classification and arm movement mapping

When using the *classification* electrode configuration, a SMR classifier was trained in a first phase with a protocol in which the user was instructed to imagine 40 times either a right or left arm movement for 8 sec. Subsequently, the g.BSAnalyze library was used to apply a Linear Discriminant Analysis to the data of each subject to classify a 2 dimensional vector data measured from the 2 lateralized bipolar deviations into either left or right arm movement imagery.

The classifier delivers a single value that indicates the distance of the current EEG readings to the decision plane, being either positive or negative depending on the classification result (left or right motor imagery). The larger the distance from the decision plane the more certain the decision. Subsequently, a moving average was applied to the classifier output to compute the data baseline and correct the data for slow drifts. A confidence threshold was implemented after the corrected data to make sure that only detections that have a minimum confidence – are at least at a minimum distance from the classification plane – would be reported. The BCI system reports 3 values: no movement detected, right arm movement or left arm movement. The percentage of time in a given time window that an arm movement is detected defines the amount of arm extension. 100% of the time of either right or left arm movement detection translates to full extension of the virtual arm. Here we define a non-extended arm as having the end effector close to the body, and full-extended as complete lateral extension. Therefore, the virtual arm movement range allows reaching an object in any position of the peripersonal space. The virtual arm movement data is low-pass filtered to ensure smooth movement transitions. Finally, the position data of the virtual arms are sent online to the VR environment by means of a UDP network connection.

### C. Experimental design

Although there have been some approaches with motor activity and imagery tasks, it is not yet clear what, if any, specific benefits of a combined approach could bring. To address this question we designed two experiments. On the one hand, a *mapping* experiment was used to assess how brain activity – more specifically at the sensory-motor areas – is modulated by different training paradigms. On the other hand, a *BCI* experiment was designed to evaluate the feasibility of the system to be controlled exclusively by SMRs. 9 naïve right handed healthy participants ( $M = 26.4$   $SD = 4.2$  years old) participated in the mapping experiment and other 9 naïve right handed healthy participants ( $M = 28.3$ ,  $SD = 5.3$  years old) participated in the BCI experiment.

The *mapping* experiment consisted of four different experimental conditions. In all cases, the user sat in front of the VR setup with the above-described *mapping* EEG electrode configuration. Data on five minutes of actual arm movements tracked with a camera based tracking system while performing the “Spheroids” training game was used to create a set of pre-recorded movement sequences for the arms of the displayed avatar. Out of these sequences, one was randomly selected for each of the experimental conditions and shown to the user. The presentation order of conditions was randomized.

The four experimental conditions were the following:

1. *Passive observation* of the movements of the avatar. In this condition, the subject was asked not to perform any motor action and only observe the arm movement sequence.

2. *Motor activity* simultaneous with observation. In this condition the subject was asked to imitate the movements of the avatar, resulting in simultaneous action and observation of movements.
3. *Simultaneous motor activity and motor imagery*. In this condition the subject was asked to imitate and mentally imagine the movements of the avatar, resulting in simultaneous motor imagery and motor action.
4. *Motor imagery* simultaneous with observation. In this condition the subject is asked to imagine him/her-self imitating the movements of the avatar, resulting in simultaneous motor imagery and movement observation.

The participants of the second BCI experiment used the *classification* EEG electrode configuration. The experiment consisted of a sequence of 4 phases. First, the BCI classifier was trained (380 sec). Then, the “Spheroids” calibration phase was used to assess the level of control of the participants by requesting them to drive the virtual arms to specific locations (7 min). Subsequently, participants played the “Spheroids” training game (10 min). Finally, all participants answered a 5 point Likert scale survey (1 lowest, 5 highest) of 23 questions covering different aspects: *enjoyment* of the experience, perceived performance *learning* during task execution, level of task *ease*, level of *control* of the virtual avatar, and appropriateness of the system *configuration* (for instance, if arms were too fast or too slow).

## III. RESULTS

### A. Mapping experiment

The BCI-VR system presented here explores the idea of combining a personalized motor training exploiting brain mechanisms for action execution and observation and mental imagery as a way to engage secondary or indirect pathways to access undamaged cortico-spinal tracks. For this purpose, it is essential to assess which of the training conditions – motor activity, simultaneous motor activity and imagery, and motor imagery – is more appropriate. In the following analysis, the passive observation condition was used to measure the baseline brain activity for each of the participants.

Mean activity brain maps (power) and statistics for each frequency band ( $\alpha/\mu$ ,  $\beta$  and  $\gamma$ ) are computed for each condition (Figure 3). Since data are not normally distributed, the non-parametric Friedman’s test was used to assess the effect of experimental conditions on the mean response (synchronized neural activity) in sensory-motor areas. Individual power response values were normalized for the comparative analysis (Figure 3A). Condition effects were found significant for all frequency bands (for  $\alpha/\mu$  band  $\chi^2(2) = 4.333$ ,  $p = .0131$ ; for  $\beta$  band  $\chi^2(2) = 6.22$ ,  $p = .0446$ ; and for  $\gamma$  band  $\chi^2(2) = 6.89$ ,  $p = .0319$ ).

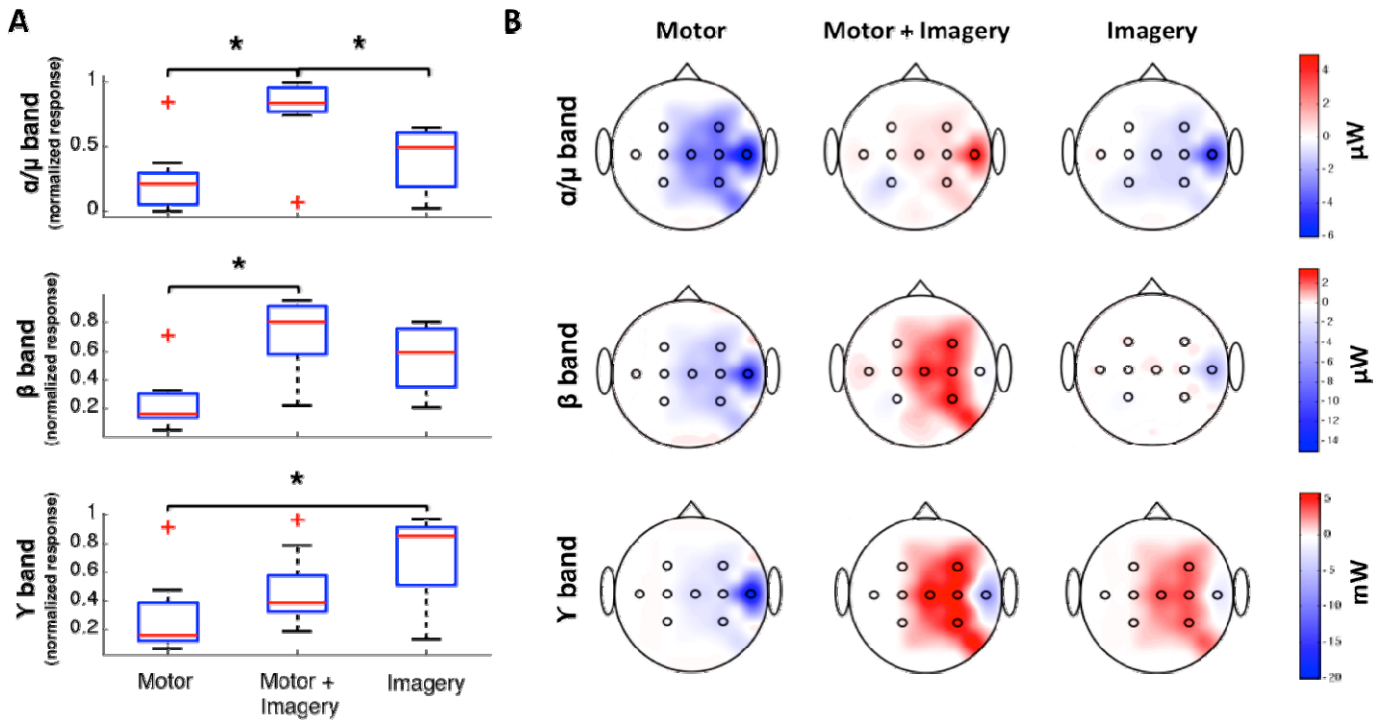


Figure 3. Analysis of brain activity for the different experimental conditions. A) Normalized mean response values for the  $\alpha/\mu$ ,  $\beta$  and  $\gamma$  frequency bands in each experimental condition. A matched pairs sign test was used for the statistical comparisons. \* indicates  $p < .05$ . The red line indicates the median and the whiskers the 5 and 95 percentiles. B) Mean brain activity maps (power) corrected with the passive observation condition as baseline. Blue indicates inhibition (lower synchronization of neural responses) and red excitation (higher synchronization of neural responses). See text for further information.

$\alpha/\mu$  band: Consistent with the literature, the motor activity condition shows the lowest response level since motor activity is generally associated with a desynchronization or inhibition of motor areas in this frequency band (Figure 3) [35]. Similarly, the motor imagery condition shows reduced neural synchronization compared to the passive observation condition (baseline). Interestingly, simultaneous motor activity and imagery shows more neural synchronization ( $Mdn = .81$ ) as compared to either the motor activity ( $Mdn = .22$ ,  $Z = 2$ ,  $p < .05$ ) or the motor imagery ( $Mdn = .52$ ,  $Z = 2$ ,  $p < .05$ ) conditions (matched pairs sign test) (Figure 3A).

$\beta$  band: Generally related to alertness or active thinking [37], and in particular hosting the SMRs, we find that the motor imagery condition is associated to a similar activation pattern as for passive observation (Figure 3B). On the contrary, the motor activity condition shows inhibited synchronization ( $Mdn = .18$ ) whereas the motor activity and imagery condition shows enhanced synchronization ( $Mdn = .81$ ), being it significantly different (matched pairs sign test,  $Z = 2$ ,  $p < .05$ ) (Figure 3A).

$\gamma$  band: Synchronous activity in this frequency band is usually attributed to cross-modal sensory processing or short term memory tasks [38]. In this case, the motor activity condition showed the lowest synchronized activity level, below the passive observation baseline (Figure 3B). Interestingly, both imagery conditions showed a bimodal

activity map, being synchronous activity enhanced in the central areas and inhibited in the right temporal lobe. Significant differences were only found between the motor activity ( $Mdn = .18$ ) and motor imagery ( $Mdn = .87$ ) conditions (matched pairs sign test,  $Z = 2$ ,  $p < .05$ ) (Figure 3A).

### B. BCI experiment

The second experiment involved 9 additional healthy participants that used the complete BCI-VR system loop. That is, they controlled the movements of the VR arms exclusively by means of the BCI interface. The goal of this experiment was to validate the functioning of the system at the technical and usability level.

The calibration phase of the “Spheroids” game was used to compute the baseline parameters for the training task and to assess the level of precision control of users when asked to move a specific virtual arm to a specific position. Data shows that participants were able to control the virtual arms above chance level (Wilcoxon signed-rank test,  $Mdn = 54.12\%$ ,  $Z = 2.8$ ,  $p = .005$ ). Chance level in this task was 1/3 given that there are 3 possible BCI classifier outputs: right arm extension, left arm extension, and no extension.

Participants were able to perform the correct movement a median of 54.12% of the time. These data contrast with the data from the “Spheroids” training game. During the game,

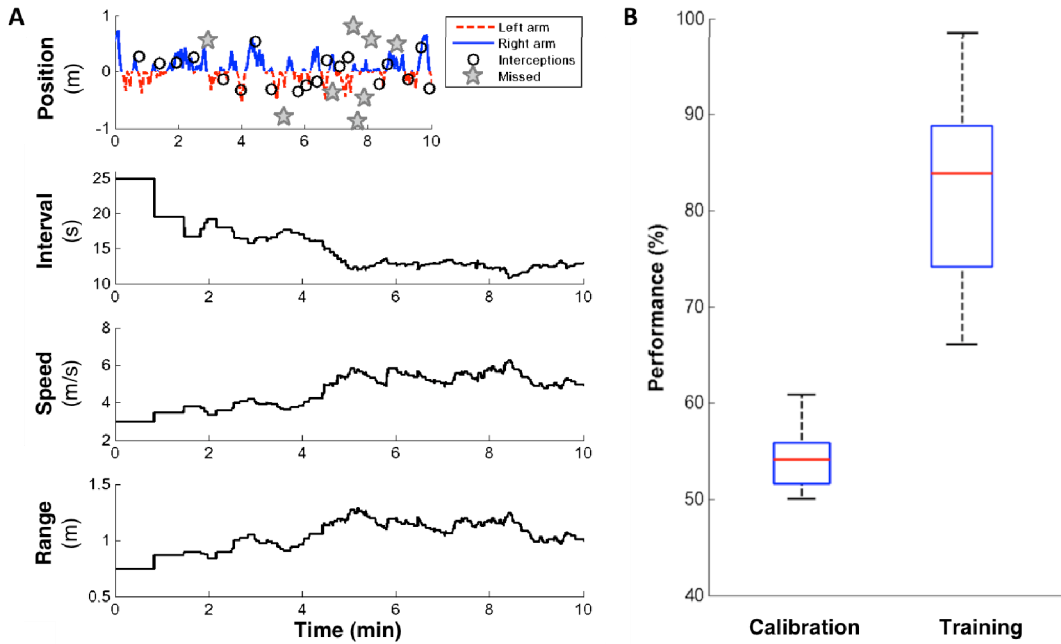


Figure 4. Analysis of the BCI controlled “Spheroids” training task. A) Topmost panel shows the arm extension values (left red, right blue) and position of game events (missed and intercepted spheres) for participant 1 during the 10 minutes of “Spheroids” training. The 3 bottom panels show the evolution over time of the mean game parameters (interval between spheres, speed of the spheres and range of dispersion). The data indicates an increase of difficulty over time (lower interval and increased speed and range) with stabilization after 5 minutes approximately. B) Performance of the users for the calibration and training tasks. Performance in the calibration is measured as % of time that the user can drive the correct arm. Performance in the training phase is computed as % of successful interceptions. Red line indicates the median and whiskers the 5 and 95 percentiles.

participants were not requested to perform a sustained reaching action over a period of time, but to perform functional control of the arms to intercept spheres (Fig. 4A, top panel). Functional performance was assessed as the percentage of correct game intercepts. The data shows that users had a better functional control than precision control over the virtual limbs, 85% in median (Fig. 4B). As consequence of the high functional control over the virtual arms, the adaptive difficulty training module implemented in “Spheroids” quickly starts increasing the difficulty of training, reducing the time interval between spheres, and increasing their speed and dispersion in the peripersonal space of the virtual avatar (Fig. 4A, bottom panels).

After the training session, participants were asked to

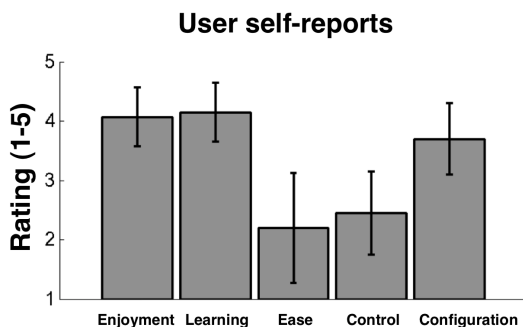


Figure 5. User experience evaluation. Users rated on a 5 point Likert scale 23 questions about enjoyment, learning, ease, control and configuration aspects of the complete BCI driven system. Bars indicate mean values and whiskers standard deviation. See text for further information.

answer a survey addressing enjoyment, learning, ease, control and configuration aspects of the complete BCI-VR system (Figure 5). Overall, participants enjoyed the training session ( $M = 4.07$ ,  $SD = 0.47$ ) and felt they had learned how to control the virtual avatar during training ( $M = 4.15$ ,  $SD = 0.49$ ). However, they found the task not easy ( $M = 2.5$ ,  $SD = 0.92$ ) and not easy to control the avatar ( $M = 2.52$ ,  $SD = 0.66$ ). In mean, participants rated the system configuration as appropriate ( $M = 3.75$ ,  $SD = 0.55$ ).

#### IV. DISCUSSION AND CONCLUSIONS

The data obtained during the mapping experiments are consistent with previous studies. Activity in the  $\alpha$  frequency band is generally associated with aspects such as relaxation, closed eye-lids and - the most importantly for the purpose - desynchronization is associated with inhibition control or motor responses (see [39] for review). Activation of this band in sensory-motor areas has been related to the resting state of motor neurons and desynchronization has been observed during motor activity and motor imagery. Largely overlapping with the  $\alpha$  band we have the  $\mu$  band. Suppression of activity in the  $\mu$  band has been recently associated with activation of mirror neurons [40]. In our experimental design we have used 4 experimental conditions - passive observation, motor activity, motor imagery and simultaneous motor activity and imagery - that

are all designed to activate the MNS to some extent. Therefore, inhibition in this band can not be directly attributed to the activation of the MNS. Instead, the role of the  $\alpha$  band in inhibition control of other brain areas can be the most probable explanation to the supra-additive interaction found in the simultaneous motor activity and imagery condition ( $p < .05$ ) (Fig. 3A, top panel). Thus, data suggests that the enhanced activation of brain areas in this condition is an indicator that the simultaneous motor activity and imagery condition is able to desinhibit additional systems than those exclusively dedicated to the generation and control of motor actions (Fig. 3A).

According to the literature, data on the  $\beta$  band contains the SMRs and correlates with active concentration, busy and alertness [39]. If correct, the brain map measured in the imagination condition indicates a similar level of concentration or alertness as for passive concentration (Fig. 3A, middle panel). Instead, the motor activity condition seems to reduce the level of alertness and concentration, being significantly lower than that of the simultaneous activity and imagery condition ( $p < .05$ ). Thus, the latter condition seems to engage more the user in the training task, maintaining or stimulating concentration to a larger extend.

Finally,  $\gamma$  activity has been observed during cross-modal processing and binding [38], and associative learning [41]. Since associative learning in the "Spheroids" task is not required, and even if it was, it would be present in all conditions; changes in the power of this frequency band are most likely due to cross-modal data processing and binding. Data shows that both imagery conditions are able to enhance cross-modal processing to a larger extend, and more remarkably in the motor imagery condition ( $p < .05$ ) (Fig. 3A, bottom panel). Given the absence of tactile, sound or force feedback during the interaction with the spheres, the data could indicate that imagery conditions are able to simulate some of those missing modalities. If correct, that would mean that imagery conditions are more appropriate for engaging additional sensory-motor systems than those directly stimulated by our VR system.

Overall, there was a larger modulation of the activity of the right brain hemisphere for all frequency bands. This could be related to asymmetries induced by the dominant brain hemisphere. In particular, this is consistent with results that support the existence of a transcallosal inhibition from the left to the right hemisphere capable of overwhelming the activity of the right hemisphere [42].

To summarize, the data shows that imagery conditions are more appropriate for recruiting cross-modal networks ( $\gamma$  band). Additionally, the simultaneous motor activity and imagery condition engages user's attention and concentration to a larger extend ( $\beta$  band). Finally, the data suggests that the motor activity and imagery condition is able to desinhibit additional networks that are not related to the generation of movements per se ( $\alpha/\mu$  band). Therefore we can conclude that, at least for our training task, a combined motor and imagery paradigm is able to recruit

more task-related networks than the rest of conditions. This means that additional secondary networks will be activated to a larger extend, allowing their recruitment for a functional reorganization to achieve improved motor control.

The second experiment has shown that a BCI setup with 2 bipolar deviations is sufficient to detect SMRs and use those signals to control an avatar in a VR environment. Although precise control of arm position is difficult (Fig. 4B), users had a high functional control of the arms, achieving a median score of 85%. Moreover, we have shown that the BCI driven system is able to online adapt to the user's capabilities, providing thus a more personalized and motivating training. User self-reports show a high degree of acceptance of the complete BCI-VR loop (Fig. 5). Enjoyment and learning are the best rated aspects (4.07 and 4.15 respectively).

Our paper has presented the rational and development of a hybrid BCI-VR neurorehabilitation system that can be used by a wide range of patients, from fully immobilized to those with a high degree of motor control. This allows the system to be deployed starting just few days after stroke, when the brain is undergoing most plastic changes. The experimental data supports the use of a dual motor activity and imagery paradigm to recruit secondary systems more effectively. These results are promising and important for the development of future neuro-feedback rehabilitation systems. In addition, we have validated the system with a full imagery based paradigm. In future experiments the system will incorporate a dual motor activity and imagery paradigm. In this future training paradigm, the movements of the avatar in the VR scenario will be modulated by both motor and imagery modalities.

In addition to the here presented training paradigm, the BCI-VR system provides us with brain activation maps that can be used to monitor the level of functional reorganization. This becomes essential in a neuro-feedback paradigm since a priori it is not known what the "right" map reorganization is. In fact, in severely affected patients it has been found that recovery is usually accomplished by recruiting contralateral networks, whereas in patients showing the higher recovery level it is by means of ipsilateral networks [43]. Hence, future systems should be able to diagnose and provide an appropriate neuro-feedback paradigm priming either ipsilateral or contralateral reorganization depending on the patient's prognostic.

## REFERENCES

- [1] WHO, *The global burden of disease: 2004 update*. 2008, World Health Organization.
- [2] Mathers, C.D. and D. Loncar, *Projections of global mortality and burden of disease from 2002 to 2030*. PLoS Med, 2006. **3**(11): p. e442.
- [3] Nudo, R.J., *Postinfarct cortical plasticity and behavioral recovery*. Stroke, 2007. **38**(2 Suppl): p. 840-5.

- [4] Murphy, T.H. and D. Corbett, *Plasticity during stroke recovery: from synapse to behaviour*. Nat Rev Neurosci, 2009. **10**(12): p. 861-72.
- [5] Seitz, R.J., et al., *Reorganisation of cerebral circuits in human ischemic brain disease*. Restor Neurol Neurosci, 2004. **22**(3-5): p. 207-29.
- [6] Sabatini, U., et al., *Motor recovery after early brain damage. A case of brain plasticity*. Stroke, 1994. **25**(2): p. 514-7.
- [7] August, K., et al., *fMRI analysis of neural mechanisms underlying rehabilitation in virtual reality: activating secondary motor areas*. Conf Proc IEEE Eng Med Biol Soc, 2006. **1**: p. 3692-5.
- [8] Bhatt, E., et al., *Effect of finger tracking combined with electrical stimulation on brain reorganization and hand function in subjects with stroke*. Exp Brain Res, 2007. **182**(4): p. 435-47.
- [9] Liepert, J., et al., *Motor cortex plasticity during constraint-induced movement therapy in stroke patients*. Neurosci Lett, 1998. **250**(1): p. 5-8.
- [10] Rizzolatti, G. and L. Craighero, *The mirror-neuron system*. Annu Rev Neurosci, 2004. **27**: p. 169-92.
- [11] Altschuler, E.L., et al., *Rehabilitation of hemiparesis after stroke with a mirror*. The Lancet, 1999. **353**: p. 2035-2036.
- [12] Cameirao, M.S., S. Bermudez i Badia, and P.F.M.J. Verschure, *Virtual Reality Based Upper Extremity Rehabilitation following Stroke: a Review*. Journal of CyberTherapy & Rehabilitation, 2008. **1**(1): p. 63-74.
- [13] Ertelt, D., et al., *Action observation has a positive impact on rehabilitation of motor deficits after stroke*. Neuroimage, 2007. **36** Suppl 2: p. T164-73.
- [14] Merians, A.S., et al., *Innovative approaches to the rehabilitation of upper extremity hemiparesis using virtual environments*. Eur J Phys Rehabil Med, 2009. **45**(1): p. 123-33.
- [15] Broeren, J., et al., *Assessment and training in a 3-dimensional virtual environment with haptics: a report on 5 cases of motor rehabilitation in the chronic stage after stroke*. Neurorehabil Neural Repair, 2007. **21**(2): p. 180-9.
- [16] Todorov, E., R. Shadmehr, and E. Bizzi, *Augmented Feedback Presented in a Virtual Environment Accelerates Learning of a Difficult Motor Task*. J Mot Behav, 1997. **29**(2): p. 147-158.
- [17] Prasad, G., et al. *Using motor imagery based brain-computer interface for post-stroke rehabilitation*. in 4th International IEEE/EMBS Conference on Neural Engineering. 2009: IEEE.
- [18] Daly, J. and J. Wolpaw, *Brain-computer interfaces in neurological rehabilitation*. The Lancet Neurology, 2008. **7**(11): p. 1032-1043.
- [19] Dobkin, B., *Brain-computer interface technology as a tool to augment plasticity and outcomes for neurological rehabilitation*. The Journal of Physiology, 2007. **579**(3): p. 637.
- [20] Lucca, L.F., *Virtual reality and motor rehabilitation of the upper limb after stroke: a generation of progress?* J Rehabil Med, 2009. **41**(12): p. 1003-100.
- [21] Birbaumer, N., *Breaking the silence: brain-computer interfaces (BCI) for communication and motor control*. Psychophysiology, 2006. **43**(6): p. 517-532.
- [22] Deng, J., J. Yao, and J. Dewald, *Classification of the intention to generate a shoulder versus elbow torque by means of a time-frequency synthesized spatial patterns BCI algorithm*. Journal of Neural Engineering, 2005. **2**: p. 131.
- [23] Ang, K., et al. *A clinical evaluation of non-invasive motor imagery-based brain-computer interface in stroke*. 2008: IEEE.
- [24] Gaggioli, A., et al., *A strategy for computer-assisted mental practice in stroke rehabilitation*. Neurorehabilitation and neural repair, 2006. **20**(4): p. 503.
- [25] Prabhakaran, S., et al., *Inter-individual variability in the capacity for motor recovery after ischemic stroke*. Neurorehabil Neural Repair, 2008. **22**(1): p. 64-71.
- [26] Ward, N.S., et al., *The relationship between brain activity and peak grip force is modulated by corticospinal system integrity after subcortical stroke*. Eur J Neurosci, 2007. **25**(6): p. 1865-73.
- [27] Cameirao, M., et al., *Neurorehabilitation using the virtual reality based Rehabilitation Gaming System: methodology, design, psychometrics, usability and validation*. Journal of NeuroEngineering and Rehabilitation, 2010. **7**(1): p. 48.
- [28] Rand, D., N. Katz, and P.L. Weiss, *Intervention using the VMall for improving motor and functional ability of the upper extremity in post stroke participants*. Eur J Phys Rehabil Med, 2009. **45**(1): p. 113-21.
- [29] Tzounopoulos, T., et al., *Coactivation of pre-and postsynaptic signaling mechanisms determines cell-specific spike-timing-dependent plasticity*. Neuron, 2007. **54**(2): p. 291-301.
- [30] Butefisch, C.M., R. Kleiser, and R.J. Seitz, *Post-lesional cerebral reorganisation: evidence from functional neuroimaging and transcranial magnetic stimulation*. J Physiol Paris, 2006. **99**(4-6): p. 437-54.
- [31] Butler, A.J. and S.J. Page, *Mental practice with motor imagery: evidence for motor recovery and cortical reorganization after stroke*. Arch Phys Med Rehabil, 2006. **87**(12 Suppl 2): p. S2-11.
- [32] Gaggioli, A., et al., *A strategy for computer-assisted mental practice in stroke rehabilitation*. Neurorehabil Neural Repair, 2006. **20**(4): p. 503-7.
- [33] Stevens, J.A. and M.E. Stoykov, *Using motor imagery in the rehabilitation of hemiparesis*. Arch Phys Med Rehabil, 2003. **84**(7): p. 1090-2.
- [34] Zimmermann-Schlatter, A., et al., *Efficacy of motor imagery in post-stroke rehabilitation: a systematic review*. J Neuroeng Rehabil, 2008. **5**: p. 8.
- [35] Solodkin, A., et al., *Fine modulation in network activation during motor execution and motor imagery*. Cereb Cortex, 2004. **14**(11): p. 1246-55.
- [36] Jasper, H., *The 10-20 electrode system of the International Federation*. Electroencephalography and Clinical Neurophysiology, 1958. **10**: p. 371-375.
- [37] Egner, T. and J. Gruzelier, *EEG Biofeedback of low beta band components: frequency-specific effects on variables of attention and event-related brain potentials*. Clinical Neurophysiology, 2004. **115**(1): p. 131-139.
- [38] Kanayama, N., A. Sato, and H. Ohira, *Crossmodal effect with rubber hand illusion and gamma band activity*. Psychophysiology, 2007. **44**(3): p. 392-402.
- [39] Hatsopoulos, N., *Rhythms in motor processing: functional implications for motor behavior*. Short course organized by the Society for Neuroscience "Rhythms of the Neocortex: Where Do They Come From and What Are They Good For, 2009.
- [40] Oberman, L., V. Ramachandran, and J. Pineda, *Modulation of mu suppression in children with autism spectrum disorders in response to familiar or unfamiliar stimuli: the mirror neuron hypothesis*. Neuropsychologia, 2008. **46**(5): p. 1558-1565.
- [41] Miltner, W., et al., *Coherence of gamma-band EEG activity as a basis for associative learning*. Nature, 1999. **397**(6718): p. 434-435.
- [42] Hayashi, M., et al., *Hemispheric asymmetry of frequency-dependent suppression in the ipsilateral primary motor cortex during finger movement: a functional magnetic resonance imaging study*. Cerebral Cortex, 2008.
- [43] Ward, N.S., et al., *Motor system activation after subcortical stroke depends on corticospinal system integrity*. Brain, 2006. **129**(Pt 3): p. 809-19.