Using Brain-Computer Interaction and Multimodal Virtual-Reality for Augmenting Stroke Neurorehabilitation

DOCTORAL THESIS

Athanasios Vourvopoulos

DOCTORATE IN INFORMATICS ENGINEERING
SPECIALTY IN SOFTWARE ENGINEERING

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"*Reality exists in the human mind, and nowhere else.*"

— George Orwell, 1984

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List of Abbreviations

- BCI Brain Computer Interface
- VR Virtual Reality
- EEG Electroencephalography
- fMRI functional Magnetic Resonance Imaging
- ADL Activities of Daily Living
- ANOVA Analysis of Variance
- ME Motor Execution
- MO Motor Observation
- MI Motor Imagery
- VMIQ Vividness of Movement Imagery Questionnaire
- MNS Mirror Neuron system
- MC Motor Cortex
- SSC Somatosensory Cortex
- VRMP Virtual Reality with Motor Priming
- EI Engagement Index

Abstract

Every year millions of people suffer from stroke resulting to initial paralysis, slow motor recovery and chronic conditions that require continuous rehabilitation and therapy. The increasing socio-economical and psychological impact of stroke makes it necessary to find new approaches to minimize its sequels, as well as novel tools for effective, low cost and personalized rehabilitation. The integration of current ICT approaches and Virtual Reality (VR) training (based on exercise therapies) has shown significant improvements. Moreover, recent studies have shown that through mental practice and neurofeedback the task performance is improved. To date, detailed information on which neurofeedback strategies lead to successful functional recovery is not available while very little is known about how to optimally utilize neurofeedback paradigms in stroke rehabilitation. Based on the current limitations, the target of this project is to investigate and develop a novel upper-limb rehabilitation system with the use of novel ICT technologies including Brain-Computer Interfaces (BCI's), and VR systems. Here, through a set of studies, we illustrate the design of the RehabNet framework and its focus on integrative motor and cognitive therapy based on VR scenarios. Moreover, we broadened the inclusion criteria for low mobility patients, through the development of neurofeedback tools with the utilization of Brain-Computer Interfaces while investigating the effects of a brain-to-VR interaction.

Keywords: Brain-Computer Interfaces, Virtual-Reality, Motor-Imagery, stroke, rehabilitation

Resumo

Todos os anos, milhões de pessoas sofrem de AVC, resultando em paralisia inicial, recuperação motora lenta e condições crónicas que requerem reabilitação e terapia contínuas. O impacto socioeconómico e psicológico do AVC torna premente encontrar novas abordagens para minimizar as sequelas decorrentes, bem como desenvolver ferramentas de reabilitação, efetivas, de baixo custo e personalizadas. A integração das atuais abordagens das Tecnologias da Informação e da Comunicação (TIC) e treino com Realidade Virtual (RV), com base em terapias por exercícios, tem mostrado melhorias significativas. Estudos recentes mostram, ainda, que a performance nas tarefas é melhorada através da prática mental e do neurofeedback. Até à data, não existem informações detalhadas sobre quais as estratégias de neurofeedback que levam a uma recuperação funcional bem-sucedida. De igual modo, pouco se sabe acerca de como utilizar, de forma otimizada, o paradigma de neurofeedback na recuperação de AVC. Face a tal, o objetivo deste projeto é investigar e desenvolver um novo sistema de reabilitação de membros superiores, recorrendo ao uso de novas TIC, incluindo sistemas como a Interface Cérebro-Computador (ICC) e RV. Através de um conjunto de estudos, ilustramos o design do framework RehabNet e o seu foco numa terapia motora e cognitiva, integrativa, baseada em cenários de RV. Adicionalmente, ampliamos os critérios de inclusão para pacientes com baixa mobilidade, através do desenvolvimento de ferramentas de neurofeedback com a utilização de ICC, ao mesmo que investigando os efeitos de uma interação cérebro-para-RV.

Palavras-chave: Interfaces Cérebro-Computador, Realidade Virtual, Imagética Motora, AVC, reabilitação

Σύνοψη

Κάθε χρόνο εκατομμύρια άνθρωποι υποφέρουν από εγκεφαλικό επεισόδιο με αποτέλεσμα την αρχική παράλυση, την αργή κινητική ανάκαμψη και τις χρόνιες παθήσεις που απαιτούν συνεχή αποκατάσταση και θεραπεία. Η αυξανόμενη κοινωνικοοικονομική και ψυχολογική επίδραση του εγκεφαλικού επεισοδίου καθιστά αναγκαία την εξεύρεση νέων προσεγγίσεων για την ελαχιστοποίηση των συνεπειών του, καθώς και καινοτόμων εργαλείων για αποτελεσματική, χαμηλού κόστους και εξατομικευμένη αποκατάσταση. Η ενσωμάτωση των τρεχουσών προσεγγίσεων τεχνολογίας πληροφοριών και επικοινωνίας (ΤΠΕ) και της εκπαίδευσης σε εικονική πραγματικότητα (VR) (βασισμένη σε θεραπείες άσκησης) έχει δείξει σημαντικές βελτιώσεις στον τομέα της αποκατάστασης. Επιπλέον, πρόσφατες μελέτες έχουν δείξει ότι μέσω της νοερής απεικόνισης (mental imagery) και της νευροανάδρασης (neurofeedback) οι επιδόσεις βελτιώνονται. Μέχρι σήμερα, λεπτομερείς πληροφορίες σχετικά με τις στρατηγικές νευροανάδρασης που οδηγούν στην επιτυχή λειτουργική αποκατάσταση δεν είναι διαθέσιμες, ενώ ελάχιστα είναι γνωστά για τον τρόπο με τον οποίο μπορούν να αξιοποιηθούν με τον καλύτερο τρόπο τα παραδείγματα νευροανάδρασης στην αποκατάσταση των εγκεφαλικών επεισοδίων. Με βάση τους τρέχοντες περιορισμούς, ο στόχος αυτής της έρευνας είναι να διερευνηθεί και να αναπτυχθεί ένα νέο σύστημα αποκατάστασης των άνω άκρων με τη χρήση νέων τεχνολογιών ΤΠΕ, συμπεριλαμβανομένων των διεπαφών εγκεφάλου-υπολογιστή (BCIs) και των συστημάτων VR. Εδώ, μέσα από μια σειρά μελετών, παρουσιάζουμε το σχεδιασμό του πλαισίου RehabNet, εστιάζοντας στην ολοκληρωμένη κινητική (motor) και γνωστική (cognitive) θεραπεία βασισμένη σε σενάρια VR. Επιπλέον, διευρύνουμε τα κριτήρια ένταξης για τους ασθενείς με χαμηλή κινητικότητα, αναπτύσσοντας εργαλεία νευροανάδρασης με τη χρήση BCIs, ενώ διερευνάται η επίδραση της απευθείας αλληλεπίδρασης εγκεφάλου με VR.

Λέξεις-κλειδιά: Διεπαφές εγκεφάλου-υπολογιστή, εικονική πραγματικότητα, νοερή απεικόνιση, εγκεφαλικό επεισόδιο, αποκατάσταση

Part I

Introduction

Motivation

Stroke is among the leading causes of death and long-term disability worldwide [Feigin et al., 2014, Mozaffarian et al., 2016]. Stroke mortality rates are higher each year than AIDS, tuberculosis and malaria put together[1234]. According to the World Health Organization (WHO), stroke deaths in Portugal reached a total of 12,757 or 17.01 % in 2014, being higher than the European average [5]. From those who survive, an increased number is suffering from severe cognitive and motor impairments, resulting in loss of independence in their daily life such as self-care tasks and participation in social activities [Miller et al., 2010a]. Additionally, treatment comes with a high societal cost, a burden which affects disproportionately individuals living in resource-poor countries where awareness of care and support is the lowest [Truelsen et al., 2007].

Rehabilitation following stroke focuses on maximizing the restoration of the lost motor and cognitive functions and on re-learning skills for the performance of the Activities of Daily Living (ADL). There is increasing evidence that the brain remains plastic at later stages post-stroke, meaning that there

[1] `http://www.who.int/nmh/publications/ncd_report2010/en/`

[2] `http://www.who.int/cardiovascular_diseases/publications/atlas_cvd/en/`

[3] `http://www.who.int/malaria/media/world-malaria-report-2015/en/`

[4] `http://www.unaids.org/en/resources/documents/2016/Global-AIDS-update-2016/`

[5] `http://www.who.int/gho/publications/world_health_statistics/2014/en/`

is still place for additional recovery [Page et al., 2004, Butler and Page, 2006]. To maximize brain plasticity, several rehabilitation strategies have been exploited. Those include the use of intensive rehabilitation [Wittenberg et al., 2016], repetitive motor training [Thomas et al., 2017], mirror therapy [Pérez-Cruzado et al., 2017], motor imagery [Kho et al., 2014], action observation [Eaves et al., 2016], etc.

To date, growing evidence of the positive impact of virtual reality (VR) techniques on recovery following stroke has been shown [Laver et al., 2015, Laver et al., 2012]. The use of simulated virtual environments and VR was fostered together with neuroscientific guidelines, forming the field of virtual rehabilitation. The utilization of virtual rehabilitation is considered a novel and effective low-cost approach to re-train motor and cognitive functions through strictly defined training tasks in a safe simulated environment, with proven effectiveness in the stroke population [Laver et al., 2015]. However, patients with low level of motor control cannot benefit from current VR tools due to low range of motion, pain, fatigue, etc [Trompetto et al., 2014]. Consequently, the idea of bypassing the peripheral nervous system was promoted by establishing an alternative pathway between the user's brain and a computer system. This is possible by exploiting the use of neural interfaces, such as EEG-based Brain-Computer Interfaces (BCIs). BCIs or EEG neurofeedback (EEG-NF) is a form of biofeedback that is used to improve cognitive and motor capabilities by self-modulating the power of different EEG bands. The most common type of BCI paradigm in neurorehabilitation is motor-imagery (MI) which includes the mental rehearsal of movements without any muscle activation.

By merging BCI technology with VR as a direct brain-to-virtual environment communication, induces illusions of movement to the patient by activating overlapping brain areas with actual movement. This type of closed BCI-VR neurofeedback loop, aims at mobilizing neuroplastic changes [Dobkin, 2007]. By augmenting virtual rehabilitation with BCIs, severe cases of stroke survivors suffering of flaccidity or increased levels of spasticity can be admitted to a rehabilitation program, exploiting the benefits of VR and complementing traditional rehabilitation methods. Results from previous research have proven mental practice of action to be useful in motor-imagery BCI (MI-BCI) training [Prasad et al., 2010, Pichiorri et al., 2015] by achieving the reorganization of motor networks which attain functional motor recovery [Dobkin, 2007]. MI training is leading to the activation of overlapping brain areas with actual movement, activating the mirror neuron system (MNS). Research in the MNS have shown that action observation, motor imagery, and motor imitation, share the same basic motor circuit as action execution and thus provide an additional or alternative source of motor training that may be useful to promote recovery from stroke [Binder et al., 2017, Losana-Ferrer et al., 2018]. Beneficial effects of MI in motor control have been shown [Birbaumer and Cohen, 2007a], and new paradigms have been proposed to maximize the recruitment of motor networks [Bermudez i Badia et al., 2013] thanks to the dynamic reorganization of sensory and motor cortices through neuroplasticity [Pascual-Leone et al., 2005]. Thus, MI-BCI can be a key component for motor learning and recovery.

Despite its portability, low cost and ease of use, current EEG-based BCI technology lacks high accuracy due to the poor signal-to-noise ratio, the low spatial resolution and the non-stationarity of the signals [Lotte, 2014]. Although preliminary findings in clinical trials with MI-BCI in stroke rehabilitation has already been shown, it is difficult to ascertain the efficacy of MI-BCI systems in a clinical setting because of the lack of long-term evidence to support its clinical relevance [Teo and Chew, 2014]. A major limitation with MI-BCI is a common lack of ability to produce vivid MI and reliable ERD/ERS of EEG patterns, and it is described as BCI illiteracy. This is due to the inability of the user to produce vivid mental images of movement resulting in poor BCI performance [Allison and Neuper, 2010], and hence recovery prospects. More importantly, after stroke, motor-imagery vividness is better when patients are imagining movements on the unaffected than on the affected side [Malouin et al., 2008].

Building on previous knowledge, this research aims at augmenting current virtual-rehabilitation tools and methodologies for people who cannot benefit from current systems. This is achieved by investigating brain-to-VR interaction and optimizing both system and user performance for maximizing recovery after stroke.

Background

Stroke

Cerebrovascular accidents (CVA) or strokes are caused by disruption of the blood supply to the brain. By depriving the brain tissue of oxygen and nutrients carried through the blood, within minutes, brain cells begin to die. This disruption is caused from either rupture of a blood vessel (hemorrhagic stroke) or blockage (ischaemic stroke) where in some cases is expressed as a Transient Ischemic Attack (TIA) [MacKay and Mensah, 2004, Stroke Association, 2014] (see Figure 1). TIA is caused by a temporary clot, often referred as "mini-stroke", making ischemic strokes the most prevalent (87%) type of stroke [Mozaffarian et al., 2015].

For instance, the way a person is disabled after a stroke depends on where the stroke is located in the brain and how much the brain is damaged. For example, someone who had a small stroke may only have minor problems such as temporary weakness of an arm or leg. People who have larger strokes may be permanently paralyzed on one side of their body or lose their ability to speak [Chronic Conditions (UK), 2008].

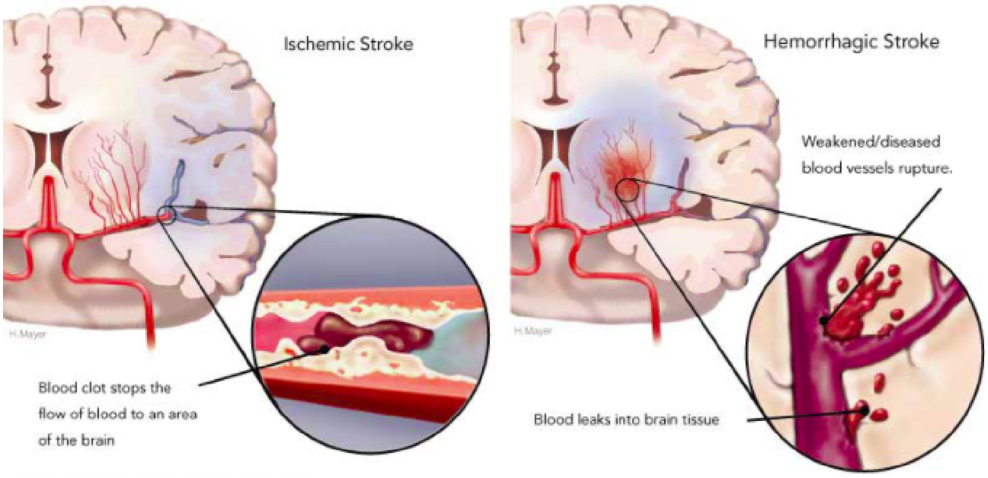


Figure 1: Ischemic and hemorrhagic strokes are two different types of stroke described in this figure. Adapted from: Heart and Stroke Foundation. (2008). Ischemic stroke.

With about 16 million new strokes per year worldwide [Strong et al., 2007], stroke has become one of the main causes of adult disability and it is expected to be one of the main contributors to the burden of disease in 2030 [WHO, 2008]. Globally, in 2013 there were 6.5 million stroke deaths, making stroke the second-leading cause of death behind ischemic heart disease [Benjamin et al., 2017].

Consequently, many stroke survivors suffer chronic conditions that require continuous rehabilitation and therapy and make them dependent on relatives, what represents a significant psychosocial and financial burden on patients, relatives and healthcare systems [Vincent et al., 2007, Gillespie and Campbell, 2011]. Recent global stroke statistics [Thrift et al., 2017] have been shown that countries with similar demographic or socioeconomic circumstances have opposing levels of stroke incidences, case-fatality and mortality rates (see Figure 2), meaning that money is not the major factor for improving stroke prevention and rehabilitation.

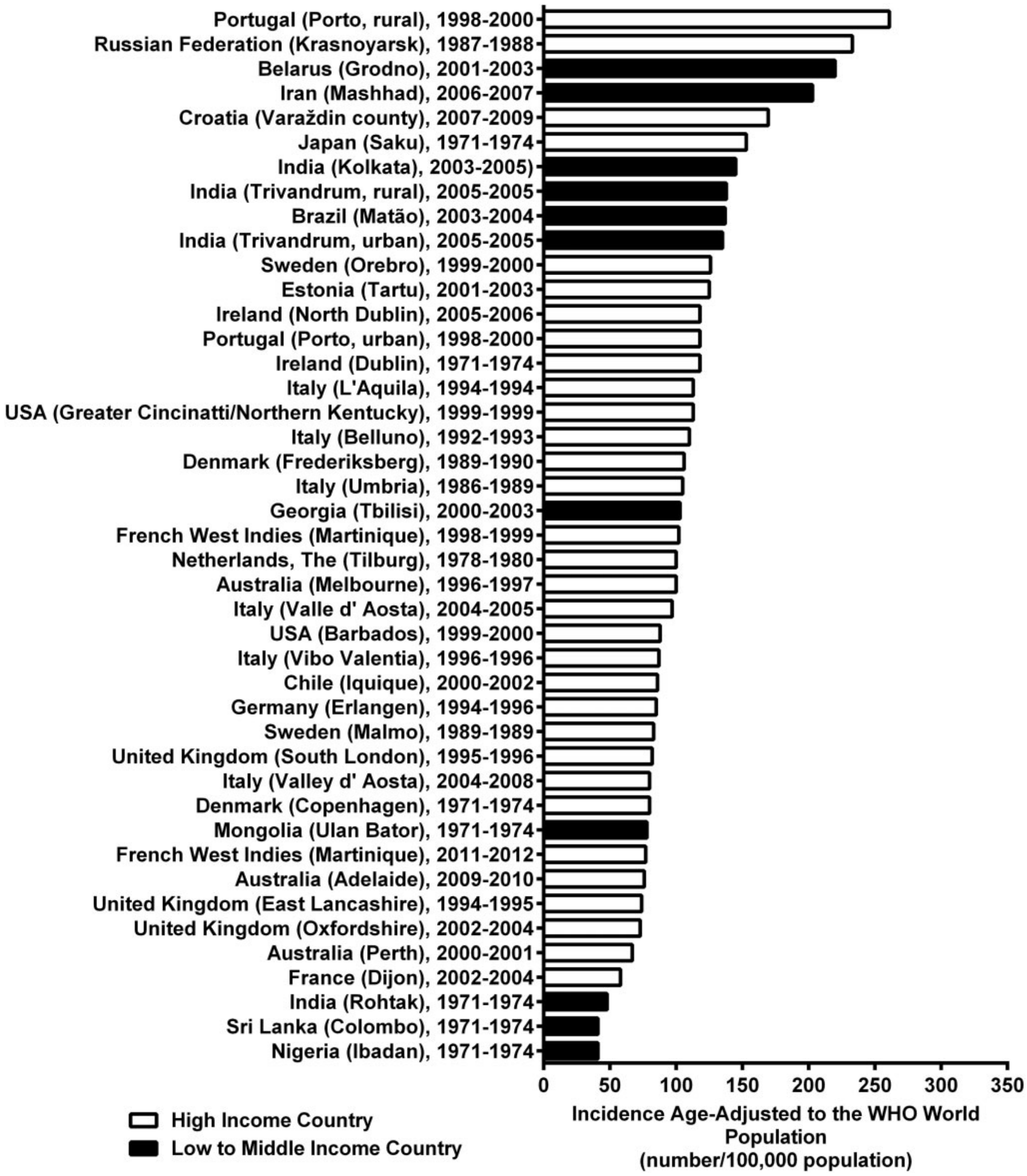


Figure 2: Incidence of stroke, adjusted to World Health Organization World population. High income countries are shown in the white bars, and low and middle income countries are shown in the black bars. Adapted from [Thrift et al., 2017]

Hence, there is a pressing need to find solutions that can help alleviate this situation with an estimated cost of 102 billion$ annual cost in the EU and USA combined [Di Carlo, 2009, Wang et al., 2014]. Moreover, recovery after a stroke is slow, and the impact of current rehabilitation approaches mostly depends on the availability of highly trained people, and access to the training frequency, intensity, and duration that are needed [Knecht et al., 2011]. Unfortunately, public healthcare systems not always can provide patients with the ideal long-term rehabilitation. Most of the therapeutic approaches are based on the exploitation of active movement (movement initiated and controlled by the patient) [Aichner et al., 2002, Hatem et al., 2016]. In patients exhibiting no active movement or high levels of spasticity in which active movement therapies are not possible, a passive movement is preferred [Van Peppen et al., 2004]. Therefore, patients with the worse prognostic (exhibiting no active movement) cannot fully benefit from active movement therapies. Current robotic approaches for upper-limb rehabilitation require a sufficient level of motor control, being only suitable for a limited subset of patients [Kwakkel et al., 2008]. Moreover, although there is data showing the effectiveness of these approaches, the specific benefits over conventional therapy remain unclear [Lo et al., 2010].

Virtual Rehabilitation

Virtual Reality (VR) can be considered a three-dimensional, computer generated environment which supports visual, auditory, and ideally touch and force-feedback display and interactive input devices (e.g. Head-Mounted Displays) [Slater et al., 2001]. During the past decades, the virtual reality community has based its development on a synthesis of earlier work in interactive 3D graphics, user interfaces, and visual simulation (see Figure 3 i).

Currently, the VR field is transitioning into work influenced by video games [Zyda, 2005]. To date, high-resolution VR managed to be mature enough for commercialization and be widely used in entertainment industry. This high-resolution VR, increased the sense of presence significantly (see Figure 3 ii). The concept of 'presence' refers to the phenomenon of behaving and feeling in VR as if we are in the physical world [Sanchez-Vives and Slater, 2005].

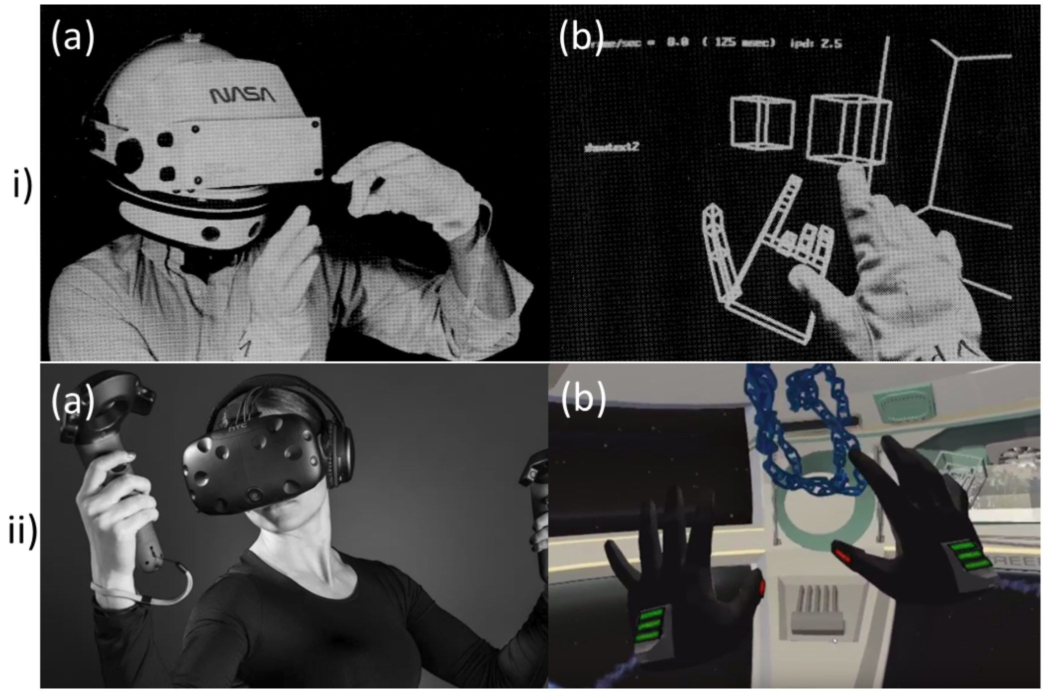


Figure 3: Old vs new. i. A 1985 NASA VR display system prototype for human factors research and telerobotics (Source: [Fisher et al., 1987]): (a) VIVED: Virtual Visual Environment Display with Data Gloves, (b) 3D graphical virtual objects and virtual hand controlled by Data Gloves. ii. State-of-the-Art Virtual Reality system: (a) The HTC Vive headset. Consumer version of the device was released on April, 2016 (Source Verge.com), (b) Weightless: A VR game with hand tracking through a mounted Leap Motion Controller (Source: https://gallery.leapmotion.com/weightless/).

In rehabilitation, VR is a particularly enabling technology that can support the requirements for an effective training. VR in stroke rehabilitation or "Virtual Rehabilitation", allows the creation of fully controlled environments that define training tasks specifically designed to target the individual needs of the patients, and intensive movement training can be embedded in motivating tasks, making use of augmented feedback and reward [Lucca, 2009].

Besides, VR based rehabilitation systems can be integrated into game-like interactions, capitalizing on motivational factors that are essential for recovery [Maclean et al., 2000]. In addition, VR not only allows for the individualization of training, self-monitoring, and monitoring by physicians, but it also enables patients to play a more active role in their rehabilitation process by taking part in the development process [Paraskevopoulos et al., 2016].

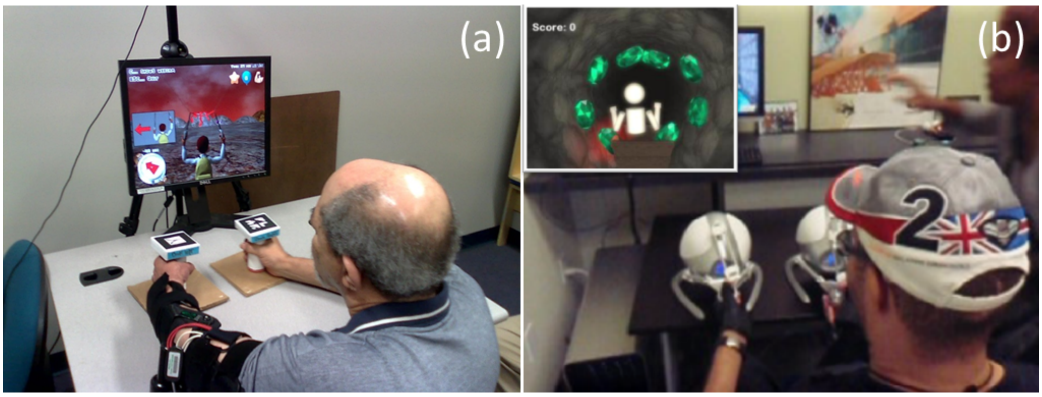


Figure 4: Examples of virtual rehabilitation systems. (a) NTT: a gamified Bimanual training system for upper-limb rehabilitation using object tracking [Bermúdez i Badia and Cameirão, 2012], (b) JewelMine: A Kinect-based rehabilitation game for upper-limb but also balance [Lange et al., 2012]

Despite evidence on the benefits of VR training [Broeren et al., 2007, Broeren et al., 2004, Cameirão et al., 2010], accessibility to these therapies still remains a challenge. This makes VR approaches suitable only to a reduced subset of patients, generally those with the better recovery prognostic. Recent meta-analyses of virtual reality studies in stroke rehabilitation included 72 trials that involved 2470 participants [Laver et al., 2017]. The latest review included 35 new studies in addition to the studies in the previous versions [Fluet and Deutsch, 2013, Laver et al., 2012]. The idea behind those systematic reviews is to provide a comprehensive review of the available evidence on a specifically identified health-related question, allowing for a rigorous analysis with limited bias. VR studies included in these reviews evaluated the effect of VR training on upper limb function, grip strength, gait speed and daily living functions. Training tasks mostly involved everyday life activities like shopping, sports activities, driving simulations and the use of public transportation simulation. In the case of upper limb re-training, 16 studies were analyzed with a total sample size of 392 patients. In most of the upper-limb studies, motion capture was used as input to the VR systems, either tracked from a camera or by using controllers with 3D space positioning such as the Nintendo Wii remote (Nintendo Co., Ltd., Kyoto, Japan). Other interface devices used in those studies are robotic devices and arm exoskeletons with position sensors. In all 16 upper-limb studies analyzed there were minimum cognitive and/or motor control requirements for the patient to interact with the VR systems and complete the desired tasks. The average Mini-mental state examination [Folstein et al., 1975] score required was as high as 21 (mild cognitive impairment) and a large percentage of studies excluded patients with perceptual deficits (43%), aphasia (35%), apraxia (29%) or pain (29%). On the motor control side, all VR systems included in these reviews for upper-limb training are based on the exploitation of active movement (movement initiated and controlled by the patient). According to the available information on the inclusion criteria, most of those studies targeted moderate-to-severe motor dysfunction ($3.3 \leq$ average Chedoke McMaster ≤ 5.5 [Valach et al., 2003]; $11.8 \leq$ average Fugl-Meyer Assessment ≤ 40 [Fugl-Meyer et al., 1975]. This makes VR approaches suitable only to a reduced subset of patients, generally those with the better recovery prognostic. Thus, these recent reviews indicate that current VR based interventions directly leave-out patients exhibiting no active movement and that most ex-clude patients with very low muscle strength, arms control, with spasticity or perceptual or cognitive dysfunction [Fluet and Deutsch, 2013, Laver et al., 2012]. This implies that patients with the worse prognostic cannot fully benefit from the novel VR based approaches for upper-limb rehabilitation, being those only suitable for a limited subset of patients. So far, even with a plethora of different VR rehabilitation systems, an accessibility problem remains. Longitudinal training studies for stroke recovery are still very rare and very difficult to implement [Karbonik et al., 2000]. To date, the specific benefits of these approaches over conventional therapy remain unclear with recent reviews indicating a statistically non-significant difference for upper limb function when comparing VR to conventional therapy [Laver et al., 2017]

Neurofeedback

For those patients with limited motor capabilities, more accessible approaches such as mental practice and neurofeedback with the use of Brain-Computer Interface (BCIs) have been shown to improve motor and cognitive task performance in some cases [Grosse-Wentrup et al., 2011]. BCIs are communication systems capable of establishing an alternative pathway between user's brain activity and a computer system. The most common signal acquisition technology in BCI is the non-invasive electroencephalography (EEG) [Wolpaw et al., 2002].

The EEG activity is distinguished by different wave patterns in the frequency domain called EEG bands or rhythms. These EEG rhythms are divided into different ranges including Delta (1 - 4 Hz), Alpha (8 - 13 Hz), Beta (13 - 30 Hz), Theta (4 - 8 Hz), and Gamma (25 - 90 Hz) while each rhythm or combination of phythmic activity is related with sensorimotor and/or cognitive states [Schomer and Silva, 2011]. For example, rhythms in the Alpha and Beta frequency bands are functionally related to major sensorimotor systems [Crone et al., 1998] which are activated primarily through motor preparation or execution [Pfurtscheller and Neuper, 1997]. Alpha and Theta oscillations are known to reflect cognitive and memory performance [Klimesch, 1999, Schack et al., 2002], and Theta was shown by early EEG studies to be closely related with problem solving, perceptual processing and learning [Schacter, 1977]. Furthermore, Delta rhythm is related to concentration, attention and internal processing [Harmony et al., 1996]. Finally, Gamma rhythm has been shown to be modulated during volitionally meditation, consciousness, and sense of self [Lehmann et al., 2001]. In addition, modulation of Gamma is observed in children with ADHD [Barry et al., 2010], in Alzheimer's Disease (AD), and also in epileptic patients [Herrmann and Demiralp, 2005]. Overall, EEG signals offer low spatial resolution measures of neural activity that occurs in the cortical area of the brain. Translating cognitive states or motor intentions from different rhythms is a complex process and is impossible to associate a single frequency range or cortical location to a brain function.

For BCIs, this oscillatory brain activity -recorded through EEG- is currently used for the interfacing between humans and computers. This communication can be triggered by an exogenous stimulus through visual, auditory or sensory feedback, like Steady State Visual Evoked Potentials (SSVEP) and P300. SSVEP is caused by visual stimulation of flashing lights and occur at the primary visual cortex of the brain [Creel, 1995] (Figure 5a). Instead, P300 responses are generated by measuring the brain evoked responses 300ms after stimulus onset (hence the name) [Guberek et al., 2009](Figure 5b).

Figure 5: Main BCI paradigms. (a) SSVEP using visual stimulation at specific frequencies through flashing lights [Guger et al., 2012], (b) P300 paradigm with evoking potentials after 300ms the desired letter appears on screen [Fazel-Rezai et al., 2012], (c) Motor-Imagery BCI training through mental rehearsal of motor movement [Jeunet et al., 2015a]

In contrast to exogenous sources, motor-imagery BCI (MI-BCI) is of endogenous origin and makes use of the visuo-motor imagination (imagination of upper and/or lower limb movement) (Figure 5c). Motor-imagery is the mental rehearsal of movement -without any muscle activation- and is a mental ability strongly related to the body or 'embodied' cognition [Hanakawa, 2015]. MI appears to largely share the control mechanisms and neural substrates of actual movement both in action execution and action observation [Eaves et al., 2014], providing a unique opportunity to study neural control of movement in either healthy people or patients [Mulder, 2007, Neuper et al., 2009] (see Figure 6). Since MI leads to the activation of overlapping brain areas with actual movement, and because sensory and motor cortices can dynamically reorganize [Lledo et al., 2006, Rossini et al., 2003], MI constitutes an important component for motor learning and recovery. Hence, MI has important benefits and is currently utilized as a technique in neurorehabilitation for people with neurological impairments [Dickstein et al., 2013].

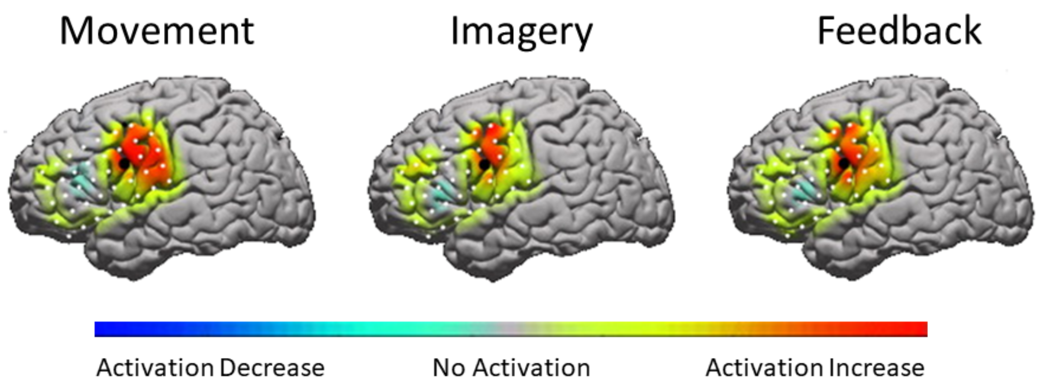


Figure 6: Electrocorticography-based (ECoG) brain activation maps for movement, imagined movement, and feedback-based BCI control of cursor, (Adapted from [Miller et al., 2010b])

In stroke rehabilitation, MI-BCI training has been the most widely used BCI paradigm [Li and Zhang, 2012]. Results from previous studies have proven mental practice of action to be useful in MI-BCI training [Prasad et al., 2010, Pichiorri et al., 2015]. MI training is leading to the activation of overlapping brain areas with actual movement, and because sensory and motor cortices can dynamically reorganize through neuroplasticity [Lledo et al., 2006, Rossini et al., 2003], MI constitutes an important component for motor learning and recovery. Moreover, research about the mirror neuron system (MNS) has shown that action observation, motor imagery, and imitation share the same basic motor circuit as action execution and thus provide an additional or alternative source of motor training that may be useful to promote recovery from stroke [Garrison et al., 2010]. Furthermore, it has been found that the spatial distribution of local neuronal population activity during MI mimics the spatial distribution of activity during actual motor movements [Miller et al., 2010b]. Beneficial effects of MI in motor control have been shown [Birbaumer and Cohen, 2007b], and new paradigms have been proposed to maximize the recruitment of motor networks [Bermudez i Badia et al., 2013].

In the last few years, the combination of BCIs with virtual environments has gained popularity, and it has been shown very useful to train functional upper limb movements [Cincotti et al., 2012, Tung et al., 2013, Spicer et al., 2017], offering a more compelling experience to the user through 3D virtual environments [Lotte et al., 2013a]. Unfortunately, sample-to-population generalizations needs big sample ($p<.05$) while so far relatively small studies are available [Chavarriaga et al., 2017].

Research Objectives

To date, although current virtual rehabilitation systems offer a plethora of assistive environments, many patients with low level of motor control not only cannot benefit from such tools rather the danger of malplasticity due to compensatory actions is imminent. Moreover, the impact of BCI-VR training is still underexplored whilst offering an opportunity for direct training of the nervous system.

This research aims at broadening modern VR rehabilitation approaches to (1) include those patients with worse prognostic (motor and cognitive); (2) provide low cost at-home rehabilitation solutions; and (3) develop a better understanding on the brain recovery process and the effectiveness derived from these solutions.

This includes the design of a novel rehabilitation paradigm, based on low cost technology which delivers motor rehabilitation for ALL patients, ANYWHERE they are, by following 2 main research objectives:

1. To develop a novel upper-limb rehabilitation system that allows us not only to effectively train motor and cognitive functions, but to monitor and to collect extensive synchronized brain activity and behavioural data on patient performance during the recovery process.

2. Generalize the findings of the research into a neurofeedback paradigm with the use of BCI's for future applications either at home or in a clinical environment

Part II

Virtual Rehabilitation

A. The RehabNet Framework

Preface

As a first objective, it is crucial the development of the foundation where a rehabilitation ecosystem can be implemented. This will allow us to effectively train stroke patients, monitor, and to collect extensive synchronized brain activity, behavioral data during the recovery process, and finally propose a complete and open platform for patients, health professionals, and engineers. To satisfy this requirement, the "RehabNet Framework" had been designed and implemented.

RehabNet Framework proposes an inclusive approach towards an open and distributed architecture for 'in-home' neurorehabilitation and monitoring by means of non-invasive ICT through neurofeedback training. In this section the RehabNet architecture is presented, its design and the implementation of a combined motor-and-cognitive system for post-stroke rehabilitation. The "RehabNet Framework" and the "RehabNet Software Suite" have been developed in the context of the RehabNet project - 'Neuroscience-Based Interactive Systems for Motor Rehabilitation' - EC (303891 RehabNet FP7-PEOPLE-2011-CIG) and is currently used for motor/cognitive training and multimodal monitoring of recovery (including brain activity, kinematic measures, and training performance data).

In the following sections, we describe all the components of the framework, presenting all the different hierarchical and abstraction layers, followed by the software implementation in terms of tools and content, showcasing the RehabNet ecosystem.

*Parts of the content of this chapter were published at:

- ***Vourvopoulos, A.***, *Faria, A. L., Cameirao, M. S., and Bermudez i Badia, S. (2013). RehabNet: A distributed architecture for motor and cognitive neuro-rehabilitation. In 2013 IEEE 15th International Conference on e-Health Networking, Applications Services (Healthcom), pages 454-459.*

Chapter 1

Developing a Distributed Architecture for Motor and Cognitive Neurorehabilitation

1.1 Approach

The RehabNet approach is based on three hierarchically organized layers (Figure 1.1): first to guarantee accessibility of patients to therapy; second to ensure patient compliance with therapy, and finally to validate the effectiveness of therapy. The main function of the accessibility layer is to provide a broad access to rehabilitation training to the wider possible range of patients. For this purpose, a number of interface and assistive technologies have been integrated, namely, physiological signals including electroencephalography (EEG), electrocardiography (ECG) and electromyography (EMG), tracking of movement kinematics including eye tracking, a robotic orthosis device with adjustable movement assistance, as well as device-independent standard interface protocols for compatibility and upgradeability of the system. Once access to therapy is granted, by the accessibility layer of RehabNet, compliance with therapy needs to be achieved. Patient's compliance with the allocated tasks and the level of engagement with the overall rehabilitation process is a challenging aspect of rehabilitation. The compliance layer aims at maximizing adherence to treatment to maximize its effect. In order to achieve this, we improve compliance by lowering the access threshold (using low-cost portable interface systems), facilitating its use by providing the rehabilitation content in the cloud, and using gaming elements to improve patient engagement. Finally, novel VR therapies need to be based on clinical guidelines and neuroscientific hypotheses of recovery. Thus, assessing the effectiveness of VR rehabilitation tools is a crucial stage for evaluating both patient's improvements and the correctness of the rehabilitation approach and the underlying neuroscientific hypotheses of recovery. It is this feedback mechanism that enables us to adjust all the appropriate elements of VR training towards the direction of a successful rehabilitation path. It is at this layer that patients interact with motor and cognitive rehabilitation VR training games, while data gathering can provide a further understanding of the underlying recovery process mechanisms.

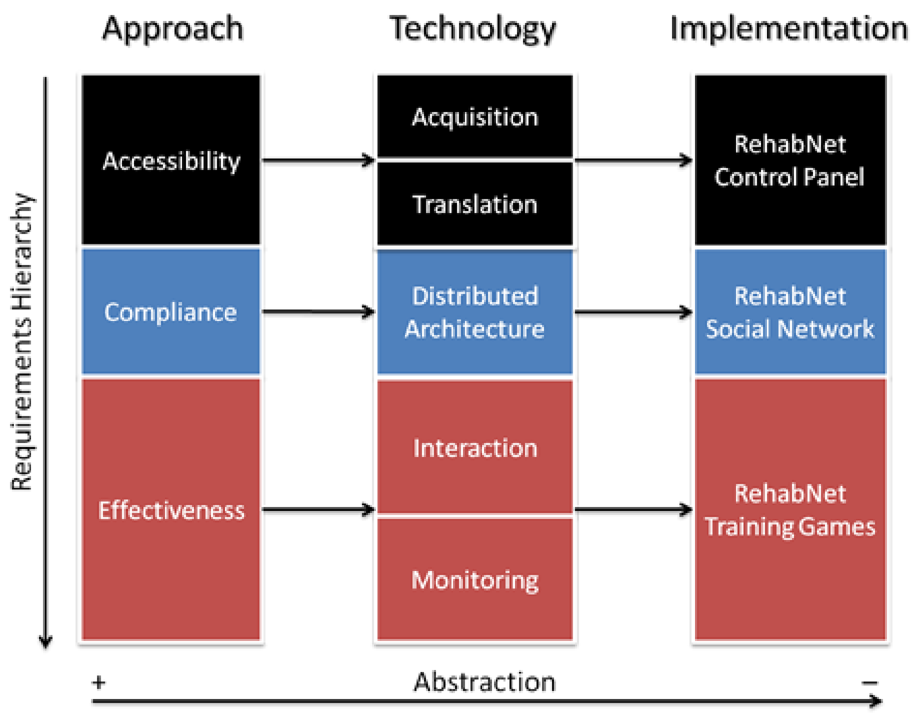


Figure 1.1: The RehabNet Framework, including the requirements hierarchy from top to bottom and the level of abstraction is from left to right.

Given the existence of novel low-cost portable technologies such as body tracking or EEG systems, RehabNet embraces the use of such technology together with the latest research findings for effective stroke rehabilitation to provide simpler and portable neurorehabilitation. Technology must offer low cost, off-the-shelf components for data acquisition; lowering the access threshold for patients with different prognostics, and targeting in-home rehabilitation. This offers new treatment possibilities to a wider range of stroke patients, including those with the most severe motor deficits. The RehabNet system architecture is built around some key concepts as it is illustrated in Figure 1.2.

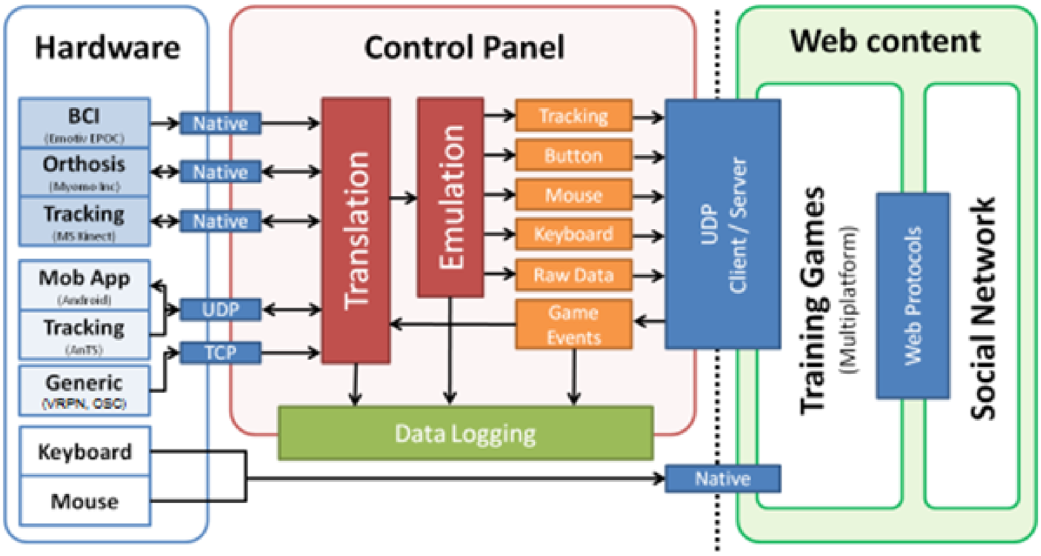


Figure 1.2: The RehabNet system architecture consists of three main building blocks: Hardware for device support, Control Panel for data translation and emulation, and Web Content for accessing the rehabilitation tools. All blocks are interconnected in a client-server (open) architecture.

For a meaningful interaction between the patient and the rehabilitation process, the acquired data must be filtered, cleaned from noise, translated (e.g. from spatial coordinates to limb movement) or classified (e.g. EEG event detection) based on pre-defined rules. The most important function of this layer is to unify all the set of actions that can be captured by all the different supported devices (BCIs, tracking, smartphones, etc) into a common information and data format that can be later used by our rehabilitation applications. For instance, this layer is in charge of classifying EEG data into left or right-hand movement and consequently emulating key presses or analog tracking devices. Similarly tracking devices like MS Kinect can also emulate button clicks and events based on kinematic parameters. Finally, orientation and acceleration data from smartphone devices can be used to emulate tracking device data.

One of the goals of RehabNet is that our rehabilitation tools have to be accessible from everywhere, both geographically (cloud services) and technologically (platform independent). Thus, the system architecture is distributed for maximum flexibility and upgradability and targeting in-home rehabilitation making use of the existing technology at home. The typical installation includes the available hardware (HW) based locally on the patient's computer. This HW can range from a simple keyboard to a BCI. If the local computer is equipped with HW other than a keyboard or a mouse, the user needs to execute the RehabNet control panel software for interfacing the HW with our rehabilitation tools. Our VR rehabilitation software is accessible online as Serious Games through a standard web browser. The use of web technologies allows patients and clinicians to have access from everywhere but additionally eases the maintenance and upgradeability at a technical level. Finally, for achieving the best possible adherence, the rehabilitation content can be made available through a social platform for patients, clinicians, and researchers that aims at enhancing the social dynamics, communication, and monitoring of patients.

The performance assessment of the VR training games can help both clinicians and patients to get useful feedback for adjusting all the appropriate variables of training towards the correct rehabilitation path and rehabilitation approach. Moreover, RehabNet allows us to collect very valuable multimodal data (movement kinematics, EEG, EMG, training events, performance data) that will assist patient's recovery while providing a further understanding of the underlying recovery process mechanisms. Monitoring is therefore essential for developing a better understanding of the effectiveness of treatments as well as identifying their behavioral and neural correlates.

1.2 Implementation

A toolbox has been developed for implementing and satisfying the aforementioned requirements is a software suite composed by a control panel (Reh@panel), tools and training games for a combined motor and cognitive re-training.

The acquisition of data from the available hardware is supported natively for a basic range of devices including EEG: EPOC (Emotiv Systems, Australia), Mindwave (Neurosky, San Jose, California, USA), EMG: Bitalino (plux, Lisbon, Portugal), mpower 1000 (Myomo Boston, USA)) and kinematic data: MS Kinect (Microsoft, Washington, USA). The device support is extended using a client/server architecture. UDP/TCP is used for communicating with mobile devices and tracking servers for continuous data tracking. Additionally, by making use of the Virtual-Reality Peripheral Network (VRPN) protocol [Taylor et al., 2001], Lab Streaming Layer (LSL)[1] and Open Sound Control (OSC) protocol [Wright and Freed, 1997] we are enabled to acquire data from a large number of existing peripherals (trackers, button devices, haptic devices, analog inputs, sound, etc) and to extend the repository of Brain-Computer Interface (BCI) support through the OpenVibe platform [Renard et al., 2010] and BCI2000 [Schalk et al., 2004].

Reh@panel is implemented in Unity 3D (Unity Technologies, San Francisco, USA), written in C#. Reh@panel [2] acts as a device router, bridging a large number of tracking devices (see Figures 1.3, 1.4, 1.5) and other hardware with the RehabNet Training Games that we want the patient to interact with. Reh@panel implements the aforementioned communication protocols in a client/server architecture and has a native device support for:

[1] `https://github.com/sccn/labstreaminglayer`

[2] `http://neurorehabilitation.m-iti.org/tools/rehabnetcp`

1. **Electrophysiological Data**

    - **Emotiv EPOC** neuro-headset is intergrated for acquiring raw EEG data, gyroscope data, facial expressions and Emotiv's Expressiv^{TM}, Cognitiv^{TM} and Affectiv^{TM} suite.
    - **Neurosky Mindwave** EEG headset is supported for raw EEG acquisition and eSense^{TM} meters of attention and meditation.
    - **Myoelectric orthosis mPower 1000** (Myomo Inc, Boston, USA) is supported, providing 2 EMG channels and adjustable levels of assistance.
    - **Bitalino** a biosignal acquisition device supporting sensors for electrocardiography (ECG), electromyography (EMG), electrodermal activity (EDA), accelerometer, and ambient light.
    - **OpenBCI** an open source brain-computer interface platform for electrophysiological signal acquisition.

2. **Kinematics**

    - **Microsoft Kinect v1** is natively supported either by the Microsoft or OpenNI drivers.
    - **Microsoft Kinect v2** through Kinect v2 SDK.
    - **Nintendo Wii remote**, a controller with the support of accelerometer and optical sensor technology.
    - **Leap Motion** a hand tracking controller through a depth sensor.

3. **Head/face tracking**

    - **Oculus Rift** VR headset.
    - **Vuzix iWear** head mounted display.

- **faceAPI** software with head and face tracking algorithms.

4. **Eye tracking**

    - **Tobii T120** standalone eye tracker.
    - **Tobii EyeX** portable eye tracker.
    - **Eye-Tribe** portable eye tracker.

Figure 1.3: The Reh@panel main interface including three main categories, Devices, Data, Options and the online apps.

Figure 1.4: Current Reh@panel supported interfaces sorted into categories.

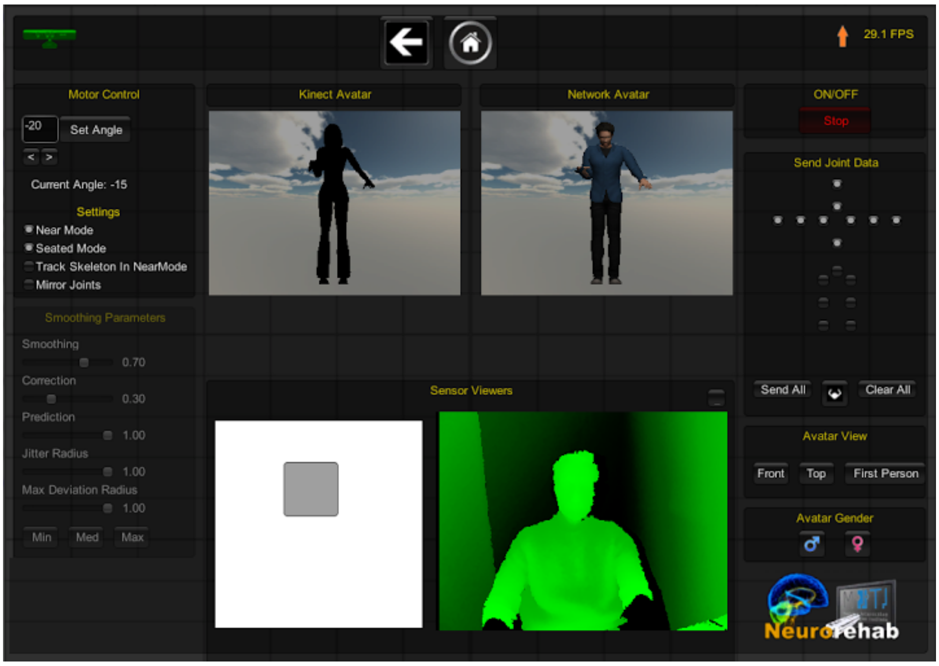


Figure 1.5: Kinect configuration panel and filtering options.

Extended device support is achieved via a custom UDP protocol (RehabNet protocol) used for bridging with external apps and devices like Reh@Mote. Reh@Mote is a mobile app for smartphones and tablets running Android OS. Reh@Mote transmits (via UDP) the available sensor data of the phone to the Reh@Panel or any other software compatible with the RehabNet protocol and it is available in Google Play store[3]. Additionally, Reh@Mote can receive data via UDP for bidirectional communication of the phone with the Reh@Panel or any Virtual Environment, enabling haptic feedback.

In addition, VRPN, LSL and OSC protocols are supported for the connection with any device (e.g. Vicon's tracking, 5DT data gloves) or software supporting it (e.g. OpenViBE BCI software, Analysis and Tracking System (AnTS), etc.)

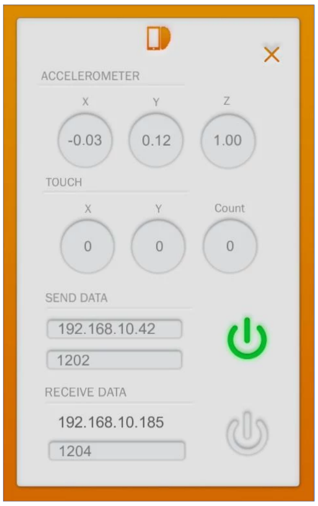


Figure 1.6: Reh@mote main UI

Reh@panel performs joint filtering (Smoothing, Correction, Prediction, Jitter Radius, and Maximum Deviation Radius) translation of the raw data into actions (e.g. hand wave, left/right swipe) and emulation (mouse/keyboard events). In addition, logging of synchronized data in XML and CSV format is configurable from all the acquisition devices and also the game events for offline analysis. Finally, Reh@panel allows to preview the translated avatar movements from the sensors, allowing to re-adjust parameters in real-time. The tool is open-source and available online for free[4].

[3]https://play.google.com/store/apps/details?id=com.RehabNet.RehaMote

[4]https://neurorehabilitation.m-iti.org/tools/en/rehapanel-overview

1.3 Usability Assessment

A Usability Evaluation was established, focusing on how well developers and game designers can learn and use Reh@panel during prototype development. This pilot evaluation was performed in the context of the Games4Health Workshop[5] at the University of Madeira, organized by NeuroRehabLab.

Games4Health Madeira Workshop purpose was to encourage students to develop prototypes of video games related to healthcare. For the usability assessment, the System Usability Scale (SUS) was distributed to all participants after the end of the workshop. SUS is a ten-item scale questionnaire, giving a global view of subjective assessments of usability [Brooke, 1996], providing an easy-to-understand score from 0 (negative) to 100 (positive).

1.3.1 Participants

The user sample was consisted by 30 undergraduate and postgraduate students (6 female) of the University of Madeira, with an average age of 25 years old (SD = 5.5) and an average computer proficiency of 4 (SD = 1) in a liker scale between 1-5.

1.3.2 Results

Overall, the total SUS score was 60/100 (Figure 1.7). Based on the adjective rating scale for SUS [Bangor et al., 2009], the system is between the "acceptable" boundaries, classified through the adjective rating as 'OK'.

[5] `https://www.facebook.com/Games4HealthMadeira/`

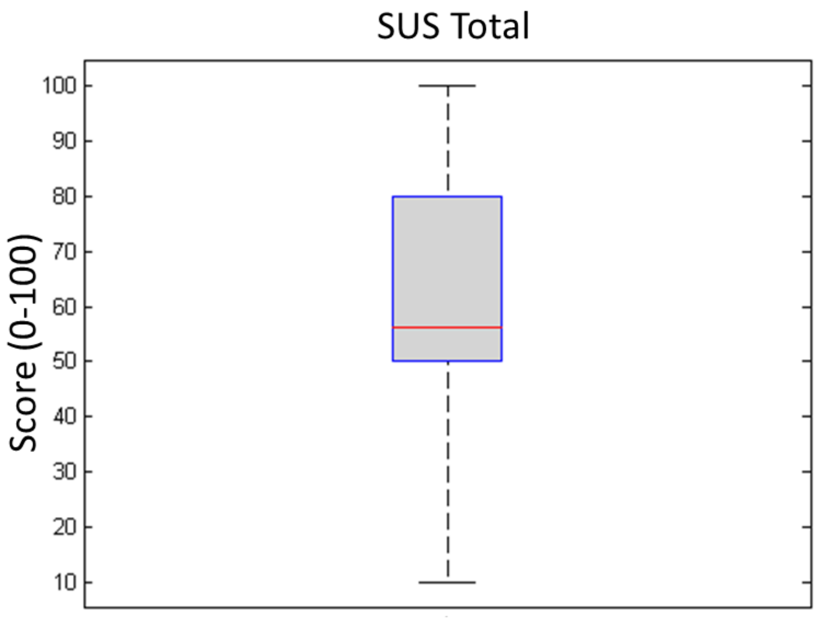


Figure 1.7: Reh@panel SUS total score

Moreover, through the SUS subscales (Figure 1.8), we can observe overall an acceptance for the system, with the majority reporting that would like to use this system frequently. In addition, the complexity is rated as low, with the learning rate kept in normal levels (getting familiar, not too fast, neither too slow). All-in-all, the system was perceived as easy to use, nonetheless, through the analysis of the comments, we updated Reh@panel into version 2.0[6] with new features. Namely, CPU usage optimization, drivers compatibility and modular architecture of the client programs for each interface.

[6] https://neurorehabilitation.m-iti.org/tools/en/rehapanel-overview

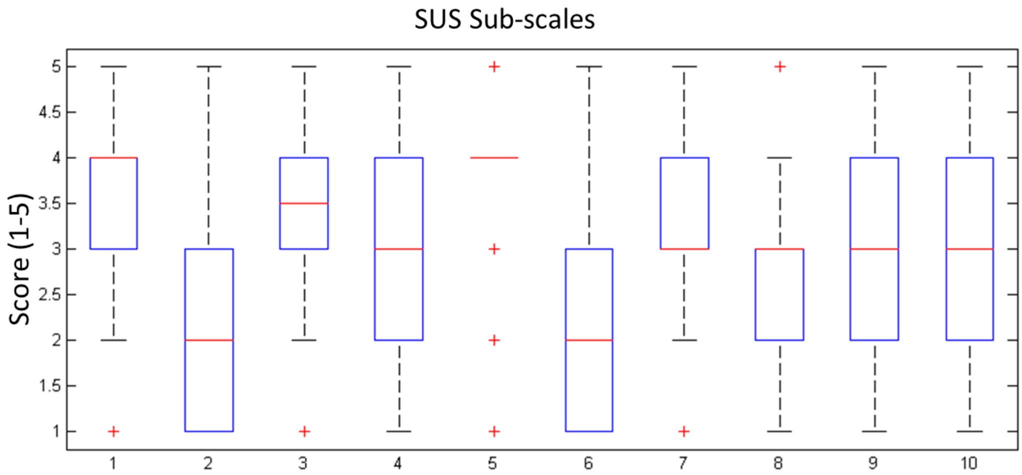


Figure 1.8: SUS subscales: 1. I think that I would like to use this system frequently 2. I found the system unnecessarily complex 3. I thought the system was easy to use 4. I think that I would need the support of a technical person to be able to use this system 5. I found the various functions in this system were well integrated 6. I thought there was too much inconsistency in this system 7. I would imagine that most people would learn to use this system very quickly 8. I found the system very cumbersome to use 9. I felt very confident using the system 10. I needed to learn a lot of things before I could get going with this system.

B. The RehabNet Training Environments

Preface

On the implementation stage, we contributed to the state-of-the-art through a set of studies in which we tried to identify current limitations in virtual rehabilitation in terms of interfaces but also training content.

In Chapter 2, we introduce the results of the effect of the different interfaces of virtual rehabilitation in patient-VR interaction. Since, little is known about how the choice of VR interfacing technology affects motor and cognitive performance but also on what the most cost-effective rehabilitation approach for patients with different prognostics is, we quantified that effect with two studies. First, we assessed the effect of four different interfaces through Reh@panel in the training of the motor and cognitive domains. For this, we have evaluated the effect of training using 2-dimensional and 3-dimensional setup, as well as traditional and natural user interfaces with both stroke survivors and healthy participants [Vourvopoulos et al., 2014a]. Secondly, improvements in terms of clinical scales (pre and post), comparing the traditional paper-and-pencil task (TP) with an adapted VR version (TPT-VR), using the aforementioned interfaces [Faria et al., 2014].

In terms of content, in Chapter 3, we introduce Rehabcity a multiplatform game designed for the rehabilitation of motor and cognitive deficits through a gamified approach to activities of daily living (ADLs). Among other findings, our results suggest that RehabCity is a valid tool for the quantitative assessment of patients with cognitive deficits derived from a brain lesion [Vourvopoulos et al., 2014b].

Finally, in Chapter 4, we assess eye gaze behavior in a VR observation task, using the RehabNet framework, in both healthy participants and stroke patients. Findings show differences in hand dominance in action observation task, differences between the constrained and non-constrained, and finally differences between paretic and non-paretic arm during action observation [Alves et al., 2016].

*Parts of the content of this chapter were published at:

- ***Vourvopoulos, A.***, *Faria, A. L., Cameirão, M. S., & Bermúdez i Badia, S. (2014). Quantifying cognitive-motor interference in virtual reality training after stroke: the role of interfaces. In 10th ICDVRAT, Gothenburg, Sweden, Sept. 2-4, 2014.*
- * ***Vourvopoulos, A.***, *Faria, A. L., Ponnam, K., & Bermúdez i Badia, S. (2014). RehabCity: Design and Validation of a Cognitive Assessment and Rehabilitation Tool through Gamified Simulations of Activities of Daily Living. In 11th International Conference on Advances in Computer Entertainment Technology. Funchal, Portugal.*
- * *Faria, A. L.,* ***Vourvopoulos, A.***, *Cameirão, M. S., Fernandes, J. C, & Bermúdez i Badia, S. (2014). An integrative virtual reality cognitive-motor intervention approach in stroke rehabilitation: a pilot study. In 10th ICDVRAT, Gothenburg, Sweden, Sept. 2-4, 2014.*
- *Alves, J.,* ***Vourvopoulos, A.***, *Bernardino, A., & Bermudez I Badia, S. (2016). Eye Gaze Correlates of Motor Impairment in VR Observation of Motor Actions. Methods Inf Med, 55.*

*Bronze Paper Award at the 11th Advances in Computer Entertainment Conference (ACE 2014), Funchal, Portugal.

*Best Paper Commendation by the International Society for Virtual Rehabilitation at the International Conference on Disability, Virtual Reality and Associated Technologies (ICDVRAT 2014), Gothenburg, Sweden.

Chapter 2

Using the RehabNet Framework to Study the Impact of Technology in Motor and Cognitive Performance

2.1 Introduction

In order to address the accessibility limitation of VR systems, approaches such as the RehabNet aim at broadening modern VR rehabilitation approaches to include patients with different prognostic (motor and cognitive) and provide low-cost at-home rehabilitation solutions for all. Our RehabNet framework and methodology are based on improving: (1) accessibility of patients to the treatment through different interfaces; (2) patient compliance with therapy with the use of VR and Serious Games; (3) understanding of the technological and neuroscientific underlying mechanisms that affect therapy's effectiveness.

However, the role and the effects of the type of interface in VR systems for neurorehabilitation are unclear with no previous literature to support the relationship between cognitive profile and type of interface. In fact, a recent review with an emphasis on evidence of VR technologies' efficacy rises concerns about the benefits of sophisticated technology for upper limb rehabilitation [Fluet and Deutsch, 2013]. Thus, the specific benefits over conventional therapy of approaches such as robots, immersive vs. non-immersive VR, and 2D vs. 3D still remain unclear. Here we address the effect of different interfaces for VR interaction in a virtual task for rehabilitation combining cognitive and upper limb motor re-training.

This research attempts to identify and understand the effect of different types of low-cost interfaces in both cognitive and motor performance in a VR task. We specifically address the effect of the nature of the interface (traditional interface vs. natural user interface), and the effect of dimensionality (2D movement on a table surface vs. 3D movement without arm support). Moreover, we present results of a comparative study between a pen-and-paper attention task with VR including healthy participants and stroke survivors using the RehabNet approach.

2.2 Methodology

2.2.1 Virtual Reality Motor and Cognitive Dual Training Task

RehabNet, was used for implementing a dual motor and cognitive training task in both a clinical and non-clinical environment [Vourvopoulos et al., 2013].

The dual VR task was inspired by a well-established cancelation task, the Toulouse-Piéron task [Toulouse et al., 2004], in the following referred as TP-VR. The VR implementation includes a first person virtual representation of the paretic arm, which is controlled via the RehabNetCP through various interfaces (see Figure 2.1). The virtual environment is composed by a grid of 25 tiles with different symbols, navigation arrows at the edge of the screen, a mini-map, and 3 target elements (out of a total of 9) in green (see Figure 2.2). By means of physical movements and the use of different interface technologies, users can control the position of the virtual paretic arm on the screen. The selection of each tile is performed with the use of a timer while the virtual arm is hovering over. Consistent with the original Toulouse-Piéron task, the score is calculated with the following formula:

$$Score = Correct - (Wrong + Omissions) * 100/TotalTiles \qquad (2.1)$$

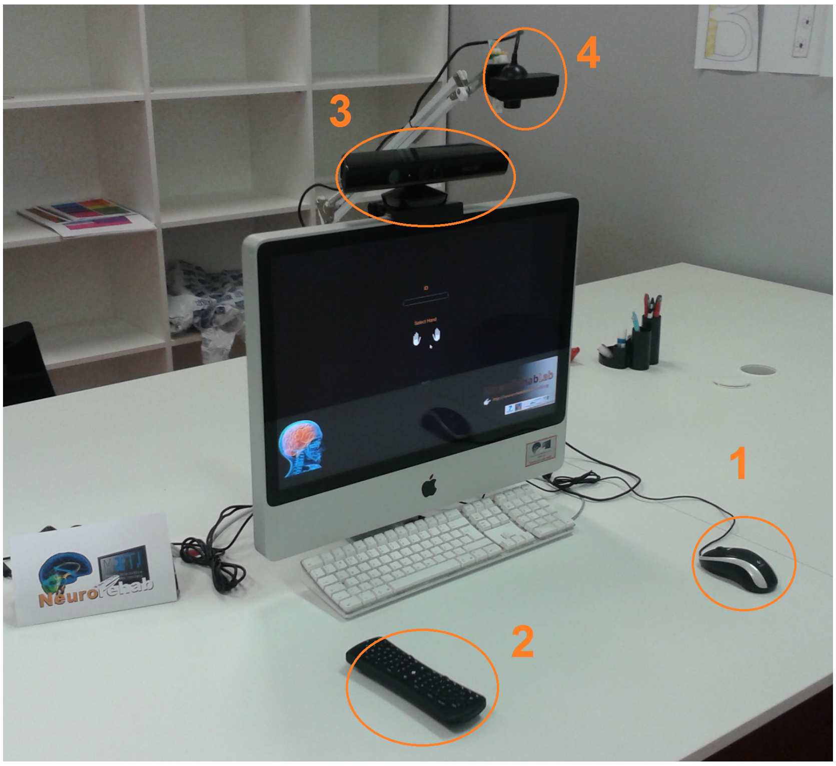


Figure 2.1: Experimental setup including the 1. mouse, 2. Airmouse, 3. Kinect, 4. camera interface

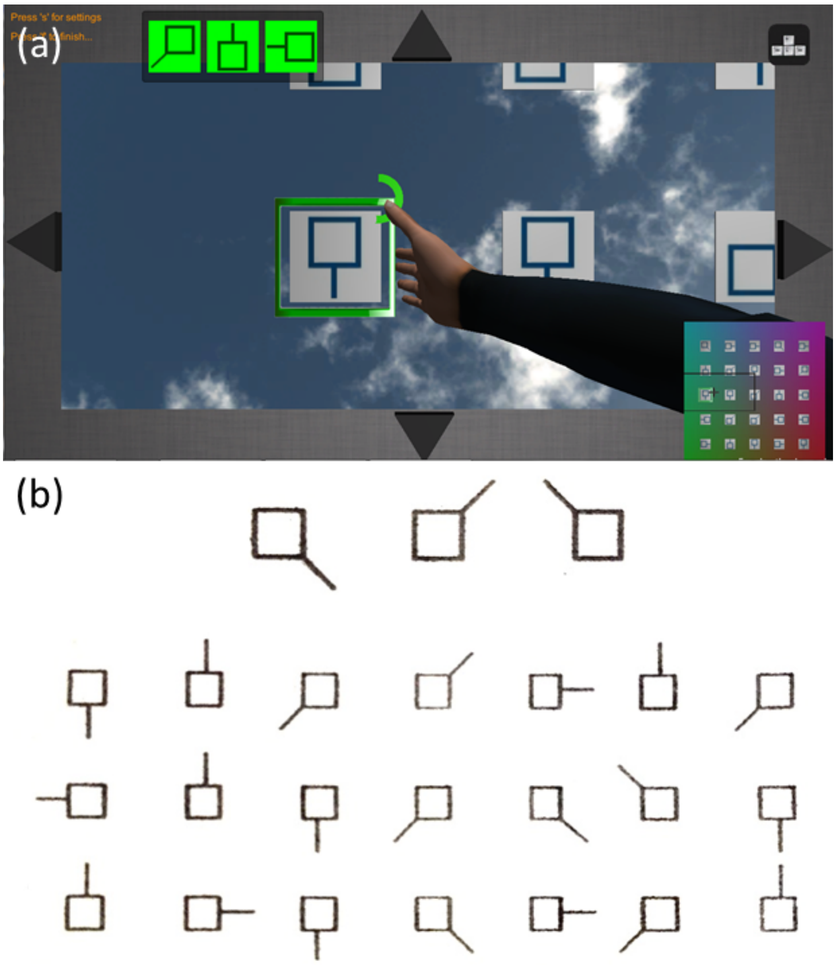


Figure 2.2: VR task compared with paper-and-pencil task. (a) Adapted Virtual-reality motor and cognitive dual-training task. (b) Toulouse-Piéron Paper-and-Pencil version

In this experiment, we decided to explore the effect of the use of Traditional Interfaces (TI) vs. Natural User Interfaces (NUI's) in 2-dimensional (Figure 2.3 a) and 3-dimensional workspaces (Figure 2.3 b). As TI we selected a 2D and a 3D pointing devices (a mouse and the Airmouse respectively), and as NUI we selected 2D and 3D camera-based tracking technologies (AnTS and Kinect respectively). In order to personalize each user interface to the capabilities of the hemiparetic arm of each patient, we developed a Range of Motion (RoM) calibration procedure. Hence, at the beginning of each session, a calibration was taking place in order to adjust the game based on the patients' RoM. Conditions were randomized within the experimental sessions with each session including one interface only. Participants have not imposed any constraint on movement type or speed.

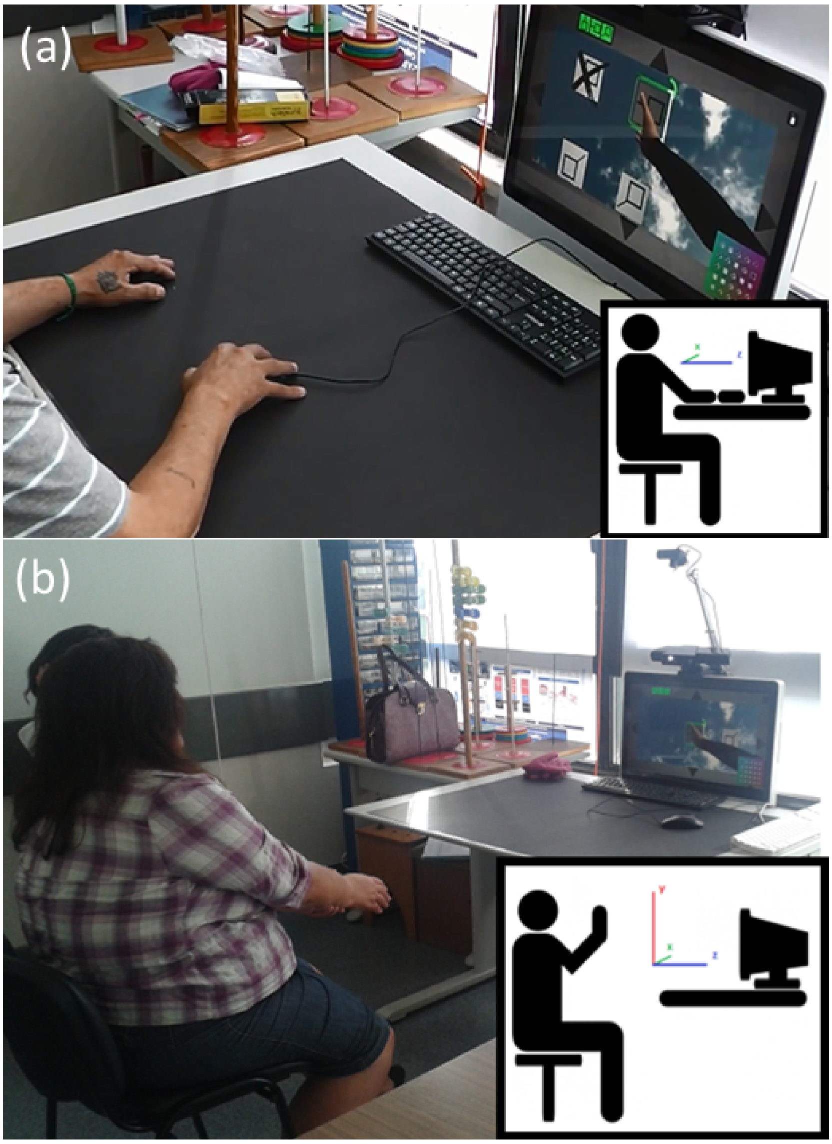


Figure 2.3: Experimental setup for 2D and 3D interaction.(a)2-dimensional experimental setup. Inset images show the user's position relative to VR system and the allowed movements. (b) 3-dimensional experimental setup. Inset images show the user's position relative to VR system and the allowed movements.

2.2.2 Experimental Setup

The experimental setup was composed by a desktop computer (OS: Windows 7, CPU: Intel core 2 duo E8235 at 2.80GHz, RAM: 4Gb, Graphics: ATI Mobility Radeon HD 2600 XT), running both the Reh@panel and the TP-VR training task. The available interfaces for this assessment included a standard mouse (TI-2D), an RC11 Airmouse (TI-3D) (Measy Electronics Co., Ltd, China), a PlayStation Eye camera (Sony Computer Entertainment Inc., Tokyo, Japan) combined with the Analysis and Tracking System (AnTS) for the tracking of a coloured glove (NUI-2D) [Mathews et al., 2007], and Kinect (NUI-3D) (Microsoft Corporation, Washington, USA). A standard keyboard was also used for baseline measurements. Data acquisition, filtering, logging were performed by the Reh@panel and sent to the virtual environment via a UDP network connection. The virtual environment was developed using the Unity 3D game engine (Unity Technologies, San Francisco, USA). For all conditions regardless of the interface being used, the Kinect skeletal tracking was also used to assess user's kinematics. Thus, Kinect provided us with rich kinematic data for all interfaces for later comparison. The procedure was transparent from the participants' point of view and they were only required to use the different interfaces for crossing out targets on the screen. For each session, the in-game data and user movement kinematics were stored for later analysis.

2.2.3 Participants

We performed a preliminary study consisting of a total sample of 66 training sessions from nine participants, three stroke survivors (1 male, 2 female), (M = 54, SD = 15) and six healthy users (4 male, 2 female), (M = 30, SD =

5.6). During a period of 1 month, each patient was exposed to an average of 12 training sessions with different interfaces, and healthy participants to 5 training sessions in one day. The clinical scales to determine the level of cognitive severity included (Table 2.1): The Addenbrooke Cognitive Examination - Revised (ACE-R) [Mioshi et al., 2006, Firmino et al., 2008] (see Appendix A), covering a wide range of cognitive impairments incorporating five subscales (attention, memory, verbal fluency, language and visuospatial capability). The clinical scales to determine the level of motor severity of the hemiparetic arm included: the Fugl-Meyer assessment, the Barthel Index. The Fugl-Meyer assessment adapted to evaluate the upper-limb [Gladstone et al., 2002](see Appendix A). Stroke patients were selected at the Physical Medicine and Rehabilitation Department of Nélio Mendonça Hospital (Funchal, Portugal) according to the following criteria: ischemic stroke; at least 2 years of schooling; stroke event with less than a year; arm hemiparesis; no hemispatial neglect; sufficient cognitive ability in order to understand the training task instructions, as assessed by the MMSE >= 15 included in the ACE-R; 45 to 85 years old and motivation to participate in the study. The six healthy participants were students and staff from the University of Madeira and were recruited at the Madeira Interactive Technologies Institute. This study was approved by the ethics committee of the Health Service of Madeira Autonomous Region and all patients signed an informed consent form.

2.3 Results

Data from 66 training sessions were gathered. Kinematics (captured through Kinect) and game data (task events in TP-VR) were synchronously logged to an XML file and parsed to MATLAB (MathWorks Inc., Massachusetts, US)

Table 2.1: Patient profile for Cognitive, Motor level and Activities of Daily Living

		Patient 1	Patient 2	Patient 3
ACE-R	Total	78	93	57
	Attention	18	18	16
	Memory	18	25	11
	Verbal Fluency	7	11	6
	Language	25	23	13
	Visuo-Spatial	10	16	11
Fugl-Meyer	Upper Limbs	50	24	48
	Sensibility	8	7	12
	Passive Movement	24	20	23
	Pain	24	16	22
Barthel	ADL	80	85	80

for analysis after each session. Kinematic data were initially cleaned from artifacts. Positional data were smoothed through Gaussian filtering window (60 seconds length, SD = 5) and the average velocity (m/s), acceleration (m/s^2), RoM (cm^2), and Smoothness Index (SI) (number of acceleration minima) was calculated. The in-game data of the TP-VR task included the overall scoring (see equation 2.2.1), the task duration (in seconds), and the number of mistakes. These data provided information of the patient's behavior within the VR environment together with the acquired movement kinematics.

2.3.1 Motor Domain

Figure 2.4 illustrates the data for both healthy and stroke participants in the motor domain (kinematic information). It can be observed that the average velocity of the patients' movements does not display differences among interfaces except for AnTS (NUI-2D), which is twice faster (0.043 m/s) compared to both 3D interfaces at (0.020 m/s) (Figure 2.4 a, i). For healthy participants there were clear differences based on the interface, being 2D interfaces slower than 3D (Figure 2.4 b, i). However, movement velocities achieved with both 3D interfaces (Airmouse and Kinect) are comparable. No differences can be observed for movement acceleration, neither patients nor healthy participants (Figure 2.4 ii).

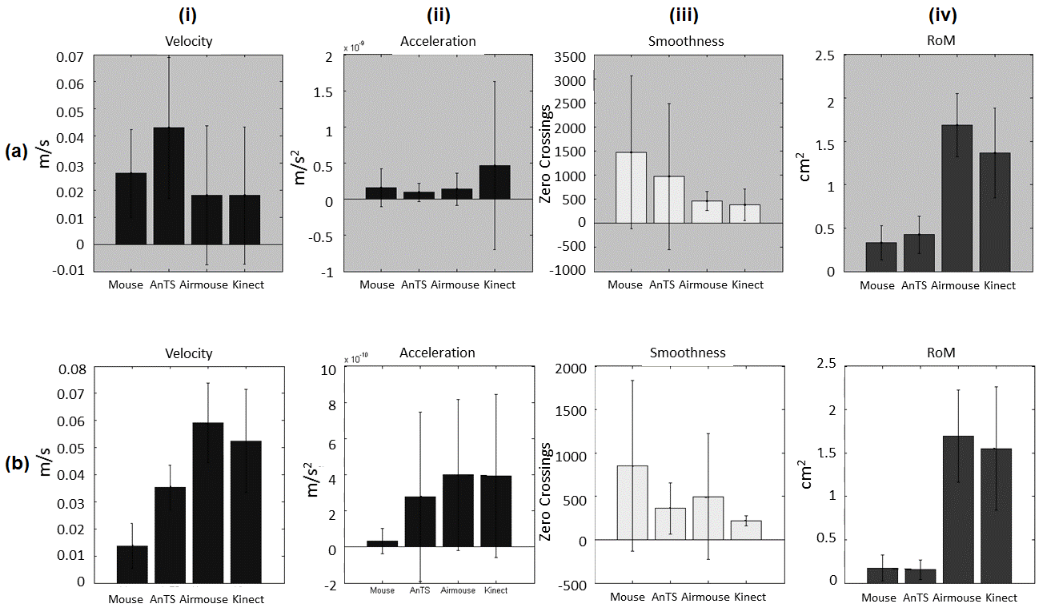


Figure 2.4: Motor domain bar-plots for (i) Velocity, (ii) Acceleration, (iii) Smoothness Index and (iv) Range of Movement (RoM) from (a) patients and (b) healthy participants. Bar height indicates mean value, and the whiskers indicate standard deviation.

As for movement smoothness, patient data shows higher SI (the higher the SI count the less smooth the movement) for 2D than for 3D interfaces (Figure 2.4 a, iii). However, a different trend is observed for healthy participants, showing smoother movements for NUI than for TI (Figure 2.4 b, iii). Finally, for RoM there is a clear distinction between the 2D vs. 3D interfaces for both patients and healthy participants (Figure 2.4, iv). In this case, 3D interfaces push participants towards wider movements that can go up to 1m larger than 2D movements.

In terms of clinical scales, at the end of the one-month intervention, we observed improvements, from pre-intervention to post-intervention, in all patients when evaluated with both the paper-and-pencil version and the

TPT-VR version although the improvements were higher in the paper-and-pencil task probably because in the VR task the motor deficits were mitigated by means of the interfaces and their calibration (Figure 2.5).

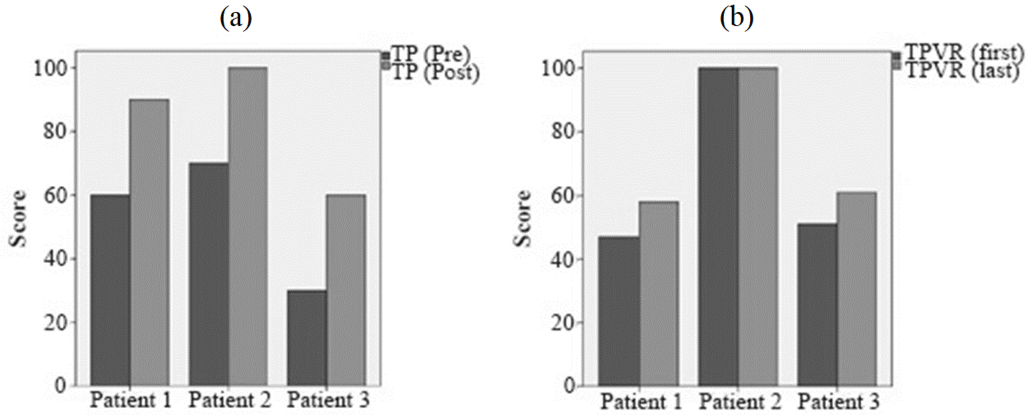


Figure 2.5: Pre and post-intervention performance in the paper-and-pencil reduced version of TP test (a) and the first and last session performance in the VR version of the TP test (b) (adapted from:[Faria et al., 2014]).

Cognitive Domain

Figure 2.7 illustrates the data in the cognitive domain for both stroke patients and healthy participants for all four tested interfaces plus the keyboard. In the case of patients, the task score is higher for both 2D interfaces (mouse and AnTS with a mean score of 64.9% and 62.2% respectively) whereas scores with 3D interfaces are close to 0 or even negative, that is, more mistakes than correct answers (Figure 2.7 a,i). Task scores for healthy participants are higher than those of patients, being NUI interfaces better compared to TI (Figure 2.7 b, i). When we analyze the time for task completion we can see that there is a clearer trend for patients than for healthy participants (Figure 2.7 ii). For patients, longer times can be found for baseline (keyboard) and

2D interfaces, being shorter towards the 3D interfaces with Kinect being the fastest. Finally, it can be seen that patients perform more mistakes when using the keyboard and the Kinect than for the remaining interfaces (Figure 2.7 a, iii). Instead, for healthy participants it can be observed that the least mistakes were on the 3D interfaces (Figure 2.7 b, iii).

In terms of clinical scales, patients improved or reached the maximum score in memory and visuospatial ability, as assessed by the ACE-R, both domains targeted by RehabNet training task. In the motor domain, we can see general improvements for patients 2 and 3. Patient 2 and 3 had improved scores as assessed by the Fugl-Meyer scale in the upper-limbs and passive movement amplitude while patient 1 had a small recess. All patients improved or maintained in the Sensibility and in the Pain scores. More importantly, all patients improved or maintained the score in the Barthel Index, meaning that this intervention had an impact in the performance of the activities of daily living in 2 of the 3 participants (Figure 2.6).

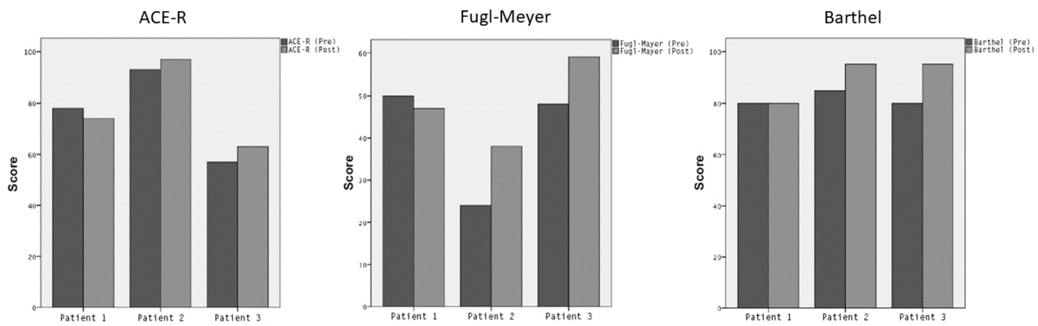


Figure 2.6: ACE-R, Fugl-Meyer (upper-limbs) and Barthel Index results showing the interdependency between the cognitive, motor and functionality variables (adapted from: [Faria et al., 2014]).

2.3.2 Interface Comparison

In order to be able to combine all motor and cognitive performance measures into a comparative analysis we ranked (between 1-4 for motor and 1-5 for cognitive, being higher a better outcome) the previously presented results Table 2.2). Thus, based on the nature of the interface (TI vs. NUI and 2D vs. 3D) we can quantify their contribution towards objective cognitive and motor performance metrics. For example, in the motor domain higher velocity, larger RoM, and smoother movement (lower SI) are desirable. Likewise, higher scores, shorter completion times and fewer mistakes are preferable in the cognitive domain.

The ranking analysis in the motor domain shows that for patients 3D interfaces are preferable in terms of acceleration, smoothness, and RoM, whereas with 2D interfaces we find the fastest movements (Table 2.2a, motor). As a result the Kinect is the best globally ranked interface (rank sum = 13). For healthy participants we find that 3D interfaces systematically provide the best motor outcomes, being the Airmouse and Kinect ranked the best with a rank sum of 14 and 13 respectively (Table 2.2b, motor). In the cognitive domain there is no clear interface outperforming the others in all metrics. 2D interfaces provide the best task scores but also the slowest task completion times (Table 2.2a, cognitive). In the case of healthy participants, there is a clear preference in the cognitive domain towards NUI (either 2D or 3D), providing both a rank sum of 12 (Table 2.2b, cognitive).

2.3.3 Multi-linear Regression Data Modelling

Following the above qualitative analysis, a more quantitative approach is necessary to understand better the impact of our experimental variables on

Table 2.2: Ranking of interfaces according to motor and cognitive performance metrics from (a) patient and (b) healthy data. The higher the ranking the better performance.

		(a) Patients					(b) Healthy				
			2D		3D			2D		3D	
		Keyboard	Mouse	AnTS	Airmouse	Kinect	Keyboard	Mouse	AnTS	Airmouse	Kinect
Motor	Velocity		3	4	1	2		1	2	4	3
	Acceleration		3	2	1	4		1	2	4	3
	Smoothness		1	2	3	4		1	3	2	4
	RoM		1	2	4	3		2	1	4	3
Total			8	10	9	13		5	8	14	13
Cognitive	Score	3	5	4	2	1	3	2	5	1	4
	Time	1	2	3	4	5	5	3	2	1	4
	Mistakes	5	3	1	2	4	1	2	5	4	4
Total		9	10	9	9	10	9	7	12	6	12

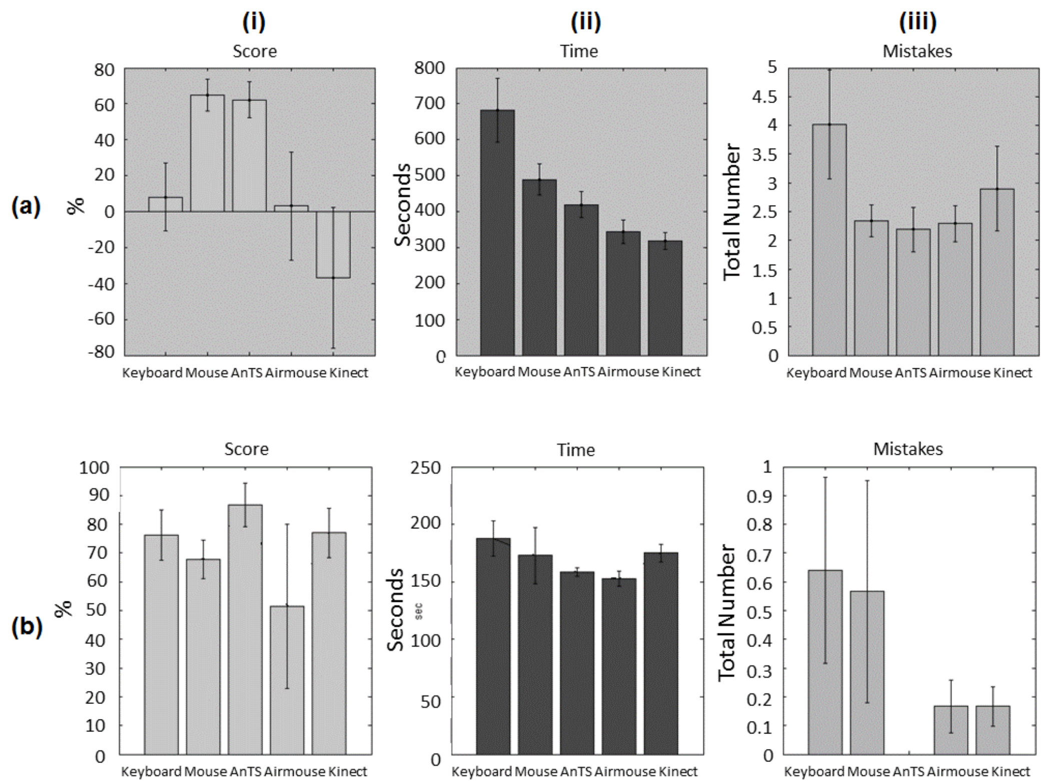


Figure 2.7: Cognitive domain bar-plots for (i) Score, (ii) Time, and (iii) Mistakes from (a) patients and (b) healthy participants. Bar height indicates mean value, and the whiskers indicate standard deviation.

the motor and cognitive domains. We decided to use a stepwise multi-linear regression modeling approach for detecting and quantifying the effect of the experimental independent variables on the dependent ones. Our independent variables include the interface, TI or NUI, and user demographics (user type, gender, age). The dependent variables in the motor domain include velocity, acceleration, the range of movement, and smoothness; and in the cognitive domain include score, time to completion and number of mistakes.

Table 2.3 summarises the modelling findings. In the motor domain we find that the dimension of the interface has a significant contribution to-

Table 2.3: Multi-linear stepwise regression model. The table shows the coefficients of the independent variables that have a significant contribution in the regression model for all metrics in the motor and cognitive domains and the R square values.

		User Type	Gender	Age	Interface	Interface Type	Dimension	R-Sq
Motor	**Velocity**						0.0295	0.52
	Acceleration	-1.58E-10						0.14
	Smoothness				-368.579			0.19
	RoM						1.5366	0.77
Cognitive	**Score**	16.3564						0.11
	Time	-114.5528						0.59
	Mistakes	-1.3194					-0.345	0.92

wards determining the velocity of the movement (Coeff. = 0.029, $p<0.001$). 3D interfaces generate faster movements, probably due to the fact that 3D movements are more ballistic in comparison to movements on a surface. The acceleration of upper limb movements is significantly affected by the type of the user (Coeff. = -1.58e-10 , $p<0.05$), were healthy participants have higher acceleration values than patients. The smoothness of movement is significantly affected by the choice interface (Coeff. = -368.58, $p<0.05$). In this case, 3D interfaces contribute towards smoother movements. Finally, the dimensionality of the interfaces (2D vs. 3D) significantly contributes to the RoM (Coeff. = 1.54, $p<0.001$). In the cognitive domain, for all dependent variables we find a significant contribution of the user type (patient vs. healthy participant): score (Coeff. = 16.36, $p<0.05$), time (Coeff. = -114.55, $p<0.001$), and mistakes (Coeff. = -1.32, $p<0.001$). It can be seen that healthy participants perform better and resolve the task faster and with fewer mistakes. Finally, we find a significant contribution of the dimensionality of the interface (2D vs. 3D) in the number of mistakes (Coeff. = -0.34, $p<0.001$), performing fewer mistakes with 3D interfaces.

2.4 Conclusions

This research aims towards the development of VR technologies for the inclusion of all patients into VR neurorehabilitation therapy, accommodating both software and hardware aspects of the technology. In this project, both stroke survivors and healthy participants have used four different computer interfaces for virtual environment interaction in order to gather insights on how the choice of the interface in a neurorehabilitation task affects outcomes in the motor and cognitive domains.

Our results indicate that patients perform faster upper limb movements by using 2D interfaces whereas healthy participants are faster by using 3D. This can be an indication that patients can interact faster when they support the paretic arm on a surface rather moving it within the 3D space, and as a result, promoting a more stable way for interaction. Consistently for patients and healthy participants, 3D interfaces contributed towards smoother movements as quantified by the Smoothness Index (SI). This could indicate that 3D interfaces generate smoother movements because there is no friction with a surface that may affect the quality of the movement. Finally, for RoM, 3D interfaces seem to contribute towards the exploitation of movements in a larger space than 2D interfaces. However, overall NUI renders better motor performance. Consequently, depending on the specific desired outcomes from training, a 2D-3D or TI-NUI interface may be preferred. In the cognitive domain, we found that better scores come at the expense of longer completion times, and shorter completion times at the expense of mistakes. Our findings verify the observed situation where the patients get tired faster when using a 3D interface, leading to faster termination of the session. Furthermore, traditional interfaces contribute towards better scoring but at the expense of poor motor performance. Consequently, the challenge is in identifying the best trade-off between the two domains in order to provide each patient with the best possible rehabilitation solution, taking into account their specific motor and cognitive re-training needs. Thus, AnTS, a 2D-NUI interface, seems to be the preferred compromise for patients. The large variability in cognitive function of the participants as assessed by the ACE-R may have been the cause of the lower accuracy of the score variable in the multi-linear regression model. However, this variability did not compromise the accuracy of the other models in the cognitive domain such as time or mistakes. Another possible limitation of the study is an eventual learning effect during the 4 week/12 sessions experimental period. Since no intermediate evaluation took place, this was minimized by randomizing the exposure to the interfaces. Finally, despite the small sample size of this pilot experiment, we believe that such a quantitative approach can provide useful pointers towards the design and deployment of future VR and rehabilitation systems taking into account both cognitive and motor domains. In this pilot study, we introduced a novel approach towards virtual rehabilitation to identify the particular benefits of interfaces and their characteristics on cognitive and motor performance. The RehabNet approach can be used to widen the spectrum of patients that can benefit from virtual rehabilitation, for in-home or clinical environments. In terms of clinical scales and despite the limitations of the sample size and amount of training, the results of this study show improvements and emphasize the value of rehabilitation approaches that merge cognitive and motor domains in single tasks. In the cognitive domain, we find improvements in domains trained by the VR task, and the generalization of the improvements to other domains in 2 of the 3 patients. However, in the cognitive domain, these improvements were small (4 and 6 points) probably due to the low frequency and intensity of the training (12 sessions of 20 minutes). The improvements in the TP paper-and-pencil task are greater than those in the cognitive domain of the TPVR task, suggesting that cognitive and motor domain improvements are related.

Chapter 3

Improving the Ecological Validity of Cognitive Rehabilitation with the RehabNet Framework

3.1 Introduction

Cognitive deficits are a major factor for loss of autonomy and independence in the performance of Activities of Daily Living (ADLs) [Cumming et al., 2013]. These deficits comprise limitations in attention (focusing, shifting, dividing or sustaining attention), executive functions (planning, organizing thoughts, inhibition, control), visuospatial ability (visual search, drawing, construction), memory (recall and recognition) and/or language (expression and comprehension). The high incidence of these deficits results from the current increase in the incidence of neurological diseases [Pritchard et al., 2013]. Every year, 15 million people suffer a stroke, 7.7 million are diagnosed with dementia and 10 million are affected with traumatic brain injury [WHO, 2008]. The loss of autonomy of the victims together with the burden of mortality and morbidity that these conditions impose on society represent a pressing public health problem. The direct costs are estimated to be more than US$800 billion per year [WHO, 2008]. Traditional cognitive rehabilitation methods typically entail a cyclical process involving: 1) assessment of the patient deficits through objective (questionnaires and scales) or/and subjective (clinical observation) tools; 2) goal setting, to define realistic and attainable goals for improvement in the patient's performance of ADL; 3) goal oriented training through the repetitive training of ADLs [Legg et al., 2007] and resolution of paper and pencil cognitive tasks; and 4) reassessment, to evaluate recovery [Langhorne et al., 2011]. The limitations of traditional rehabilitation methods evidenced the need of personalized tools that can be used more intensively by patients and therapists, in clinical or at home environments. One recent approach is the use of gaming to train motor, cognitive, and social abilities [Nap and Diaz-Orueta, 2012]. Gaming in rehabilitation has great potential for today's and future health care, and there is increasing evidence that gaming positively contributes to the recovery process of stroke [Laver et al., 2012]. Rehabilitation through computer based gaming capitalizes on motivation to engage in rehabilitation and the personalization of training [Rego et al., 2010]. Moreover, gaming enables online monitoring of performance and the possibility to provide immediate feedback in controlled settings, making it suitable for at-clinic or at-home rehabilitation [Nap and Diaz-Orueta, 2012]. Besides monitoring the performance and progress of the player, training through gaming allows the use of rehabilitation principles such as goal setting, feedback, reinforcement and self-efficacy. Finally, improvements in gaming have been found to transfer to real task performance [Dede, 2009]. Some well-established computer-based approaches replicate standard paper and pencil tasks in a computer environment, lacking the use of gaming elements. For instance, the REHACOM system is widely used in clinical environments and it targets training of several cognitive domains [Schuhfried, 1996]. Some newer approaches such as the IREX GestureTek [Guberek et al., 2009], the Neurorehabilitation Training Toolkit [Bermúdez i Badia and Cameirão, 2012], the Dance2Rehab3D [Bruckheimer et al., 2012] and the TheraGames [Kizony et al., 2006] are games that support sophisticated tracking, orienting and signaling systems for impaired people. Nevertheless, their focus is mostly on motor training game tasks that are not directly related to ADL. The main goal of rehabilitation is to re-enable people with impairments to perform effectively their ADLs [Sohlberg and Mateer, 2001], hence numerous systems were developed with the purpose of simulating the ADLs in a Virtual Reality (VR) environment. For example, the Virtual Action Planning - Supermarket (VAP-S) [Josman et al.,] trains individuals to plan a purchasing task in a virtual supermarket; the Virtual Street Crossing System [Navarro et al., 2013] recreates a real scenario of a city, for players to navigate in the presence of distractor stimuli (cars, traffic lights, sounds); and a system by Gamito et al. [Gamito et al., 2012] simulates various ADLs like morning hygiene, meal preparation, dressing, etc. Although these VR simulations are more ecologically valid than the computerization of paper and pencil tasks, these systems focus only on training specific ADLs in an isolated context. The AGATHE project followed a more holistic approach, integrating ADLs in a valid context [Klinger et al., 2013]. This system consists of a virtual neighborhood with several landmarks (town, studio, post office, supermarket), each of which is used to train specific ADLs. Although it is configurable, upgradable and able to provide personalized therapeutic training, the system lacks a gaming approach and a quantitative evaluation with end users. By merging a gaming and an integrative ADLs approach we propose RehabCity, an online deployed game for the rehabilitation of cognitive deficits. A simulated city populated with streets, sidewalks, commercial buildings, parks and cars, has been created to provide an ecologically valid environment, where some common ADLs are executed. In the RehabCity game, the player has to perform several sequential tasks that require navigation in the city. RehabCity uses short-term goals and frequent feedback on progress to increase the sense of self-efficacy and, as a result, the motivation and engagement to work towards the next goal. Furthermore, RehabCity goals can be customized and personalized to each player, as well as the level of difficulty assistance provided by the game. In this paper we present the design, implementation and validation of the Rehabcity.

3.2 Methods

3.2.1 Design

RehabCity has been designed based on a participatory approach [de Freitas and Jarvis, 2006] as an attempt to actively involve stakeholders (e.g. health professionals and patients, in our case) in the design process of the game to ensure that the result is usable and meets the user's needs. The process started by collecting standard paper and pencil training tasks widely used in clinical environments. Subsequently, together with a rehabilitation physician, we selected 12 tasks considered to have more impact in the successful performance of ADLs. In addition, 20 health professionals experienced with brain-injured patients (physicians, occupational therapists, speech therapists, neuro-psychologists and physiotherapists) provided input on how to operationalize the difficulty, memory, executive functions, attention and language demands of each task. Finally, some tasks that could be integrated through the performance of common ADLs were implemented in RehabCity, such as visuospatial orientation, attention and executive functions.

3.2.2 Implementation

Improving the ecological validity of Activities of Daily Living (ADLs) Although paper and pencil training allows for a very controlled and specific intervention in one or several cognitive domains, it lacks of an ecologically valid context. Real life activities usually involve interdependency of multiple cognitive domains. The main goal of RehabCity is to provide an integrative and engaging cognitive training experience that, not only simulates ADLs, but it tries to do so in an ecologically valid context. Thus, we recreated in VR a simulated city neighborhood of 386x358m2 to integrate the cognitive training tasks derived from the participatory design process and to deliver them, in a very controlled manner, in the context of real life ADLs. RehabCity is organized in a quasi-regular grid structure of streets with sidewalks, containing over 200 realistic buildings, several parks and moving vehicles. In this simulated city, four of the most commonly visited places by patients have been reproduced: a supermarket, a post office, a bank, and a pharmacy. Further, to increase the ecological validity, all of these places display billboards and products of real spaces and trademarks that are commonly found in Portugal. This helps the patient in relating the in-game goals to the real world. Multiple auditory and visual feedback elements are used to support the player in the accomplishment of the in-game goals as well as to reward successful actions. Points are accumulated at each goal completion (+20) and at each intermediate task (+1), and points are subtracted (-1) whenever a mistake is performed or the player resorts to a so-called "map/objective" button for additional help. The game is designed as an open-ended experience, organized in levels of predefined complexity. If a player finishes Level 1 successfully, he/she will continue onto Level 2, 3 and 4 until time is over. A final score of performance is not provided to avoid frustration and discouragement in case of negative feedback. Additionally, tasks are generated procedurally with increased difficulty to support replayability, meaning that multiple game plays with the same settings result in different game experiences. In RehabCity we have created multiple in-game tasks, organized in difficulty levels that address the following cognitive domains: visuospatial orientation, attention, and executive functions.

The experimental setup was composed by a desktop computer (OS: Windows 7, CPU: Intel core 2 duo E8235 at 2.80GHz, RAM: 4Gb, Graphics: ATI mobility Radeon HD 2600 XT) with a 24" LCD monitor, running both the RehabNet framework toolset and the RehabCity. For our testing we used an arcade type of joystick (Topway's Digi-usb Joystick Tp-usb670, China) with customized button colors corresponding to the in-game instructions. On each session, patients were placed approximately 60cm distance from the PC screen facing the center of it (Figure 3.1).

Finally, RehabCity is multiplatform[1], it was implemented using the Unity 3D game engine (Unity Technologies, San Francisco, USA) and can be accessed online. RehabCity has been developed within the RehabNet framework, which allowed us to record face position and orientation information (6 DoF) with a high-resolution webcam[2] (FaceAPI, Seeing Machines,

[1] `https://play.google.com/store/apps/details?id=com.NeuroRehabLab.RehabCity`

[2] `https://neurorehabilitation.m-iti.org/tools/en/faceapi`

Tucson, USA) for investigating gaze behavior during game performance.

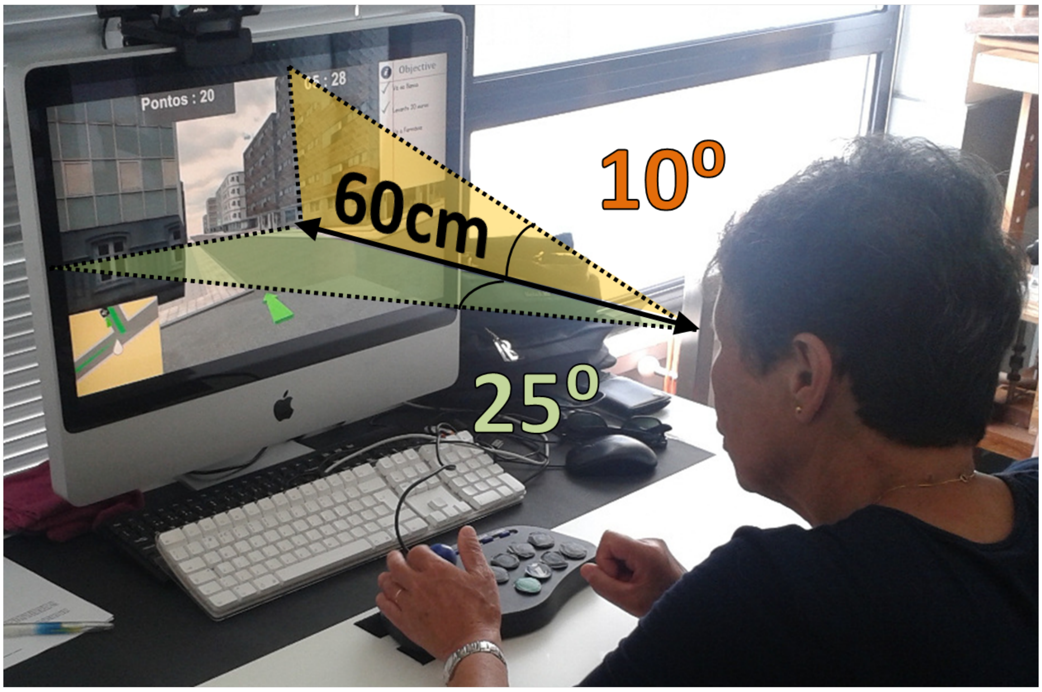
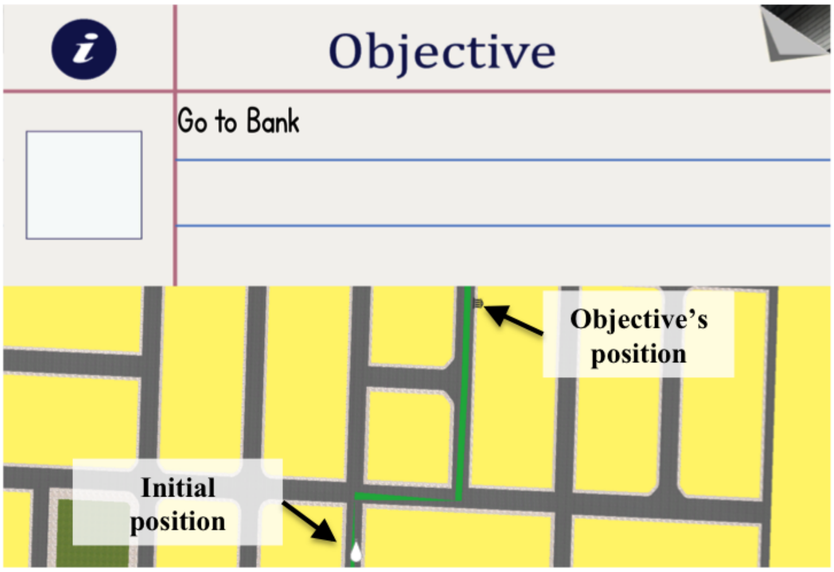
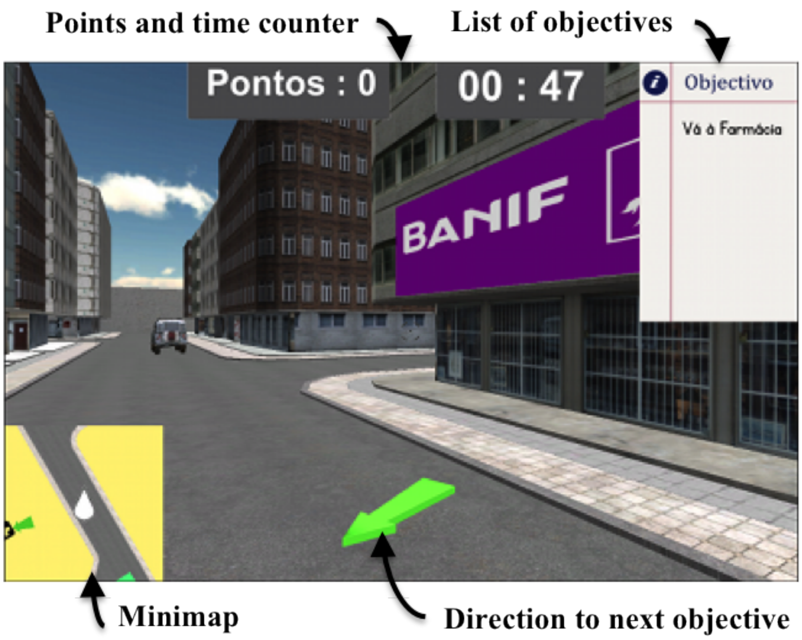


Figure 3.1: Patient positioned in front of the experimental setup during the user study. Face position and orientation is tracked by FaceAPI using the build-in webcam.

Visuospatial orientation All in-game tasks happen at specific locations in the city that are designed to reproduce real life tasks and environments. Thus, patients need to navigate through the city to go to the appropriate places for the in-game goals. Because we are dealing with patients of generally older age and low computer literacy, the city has been designed to have only square or rectangular building blocks and regular street intersections. This arrangement helps in memorizing the number of turns a player needs to take to get to destination, and allows us to control very precisely the difficulty of the task. RehabCity incorporates several in-game elements to support players with the visuospatial orientation tasks. When a goal is given to the player, a general map of RehabCity, showing in green the optimal path from the player's position to the goal, aids in the task (Figure 3.2a). These maps show only the player, streets and places, ignoring unnecessary details that can be overwhelming. A player can always use a "map/goal" button to bring up again this general map of RehabCity at the expense of in-game points. During the game, and depending on the player's needs, RehabCity can be configured to provide a mini-map in the lower half of the screen and/or a guidance arrow placed in front of the player (Figure 3.2b).



(a) In-game goal instructions supported with a map indicating the optimal path (green line)

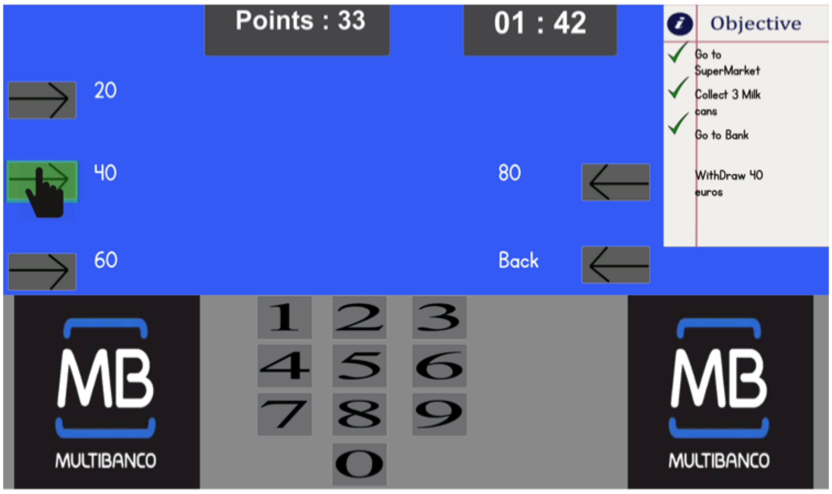


(b) First-person navigation in the RehabCity indicating the Points and Time counters, list of goals, mini-map and direction to the next goal

Figure 3.2: Navigation challenges in RehabCity

Attention RehabCity incorporates attention-training tasks related to relevant ADLs in different scenarios (supermarket, post office, bank, and pharmacy). The implementation of these tasks sits in between the more traditional paper and pencil cancellation tasks – tasks where patients need to cross out target elements among distractors – and real tasks where target and distractors are embedded in the real 3D environment (Figure 3.3a). This implementation enables us to have full control over the elements that determine the difficulty of training - such as the number and nature of target objects, number of distractors, their sizes and spatial arrangement - while avoiding navigation and interaction difficulties that can result from the exposure of patients to hyper-realistic 3D models of those places. The task parameters are then configured according to the patient's training needs, enabling the possibility to personalize training and provide both very simple and very demanding attention tasks.

(a) Simplified supermarket scenario displaying grocery products organized in shelves showing a wrong selection (left) and a correct selection (right) of an item of the goal's list



(b) In-game reproduction of a cash machine. The layout, button arrangement and options correspond to those of a real Portuguese cash machine (Multibanco).

Figure 3.3: Examples of attention and executive function training scenarios

Executive functions Executive function is a generic term that is used to designate the regulation of cognitive processes, including working memory, reasoning, problem solving and calculation, among other [Chan et al., 2008]. RehabCity is designed to pose challenges in those domains by defining a list of goals that the players have to accomplish. Goals can be simple elementary instructions – "go to the supermarket" –, a list of them – "go to the supermarket", then "buy bread and milk", etc. – or problem solving tasks of different levels of complexity – "withdraw 50 euros from the cash machine" or "get some food for breakfast" (Figure 3.3b). The later ones require the player to solve intermediate tasks that are not explicitly expressed in the goals, such as successfully selecting the right options in the cash machine or figuring out what type of food is appropriate for breakfast. The game goals are presented initially in a list that occupies the upper-half of the screen, together with the RehabCity map, that minimizes to the upper-right corner (Figure 3.2, Figure 3.3). This list supports the player by displaying the current goal and recently completed goals. The visibility of the list is configurable but the player can always access it using the "map/objective" button at the expense of game points. Through the configuration of the visibility of this list we can require the player to focus on the task at hand or to have to memorize the sequence of in-game goals.

3.2.3 User study

The study took place in the Physical Medicine and Rehabilitation Unit of the Hospital "Dr. Nélio Mendonça" in Funchal, Madeira. The recruited sample consisted of 10 patients (8 females and 2 males between 35 and 77 years old) with cognitive deficits derived from stroke, traumatic brain injury and mild cognitive impairment. Patients had between 2 to 12 years of schooling, and

4 of them had no previous experience with computers. The ethics committee of the Hospital approved the study and all participants signed a written informed consent.

Protocol In order to assess how the cognitive profile of the participants relates to game performance and acceptance, all participants performed several evaluations prior to the game experience. They were evaluated with the Mini-Mental State Examination test [Folstein et al., 1975], a well-established screening questionnaire that comprises the evaluation of orientation (time and place), attention (calculation), memory (immediate and delayed recall), language (naming, repetition and writing) and visuospatial capabilities (drawing a complex geometric figure) [Appendix A]. Additionally, the Stroke Impact Scale 3.0 – a self-reported questionnaire assessing 8 domains: motor strength, hand function, ADL's, mobility, communication, emotion, memory, thinking, and social participation [Appendix A] – was used [Duncan et al., 2003]. Training sessions with RehabCity are limited to 20 minutes to reduce fatigue, and the objective is to resolve as many goals as possible. After each session, participants rated their experience with the System Usability Scale (SUS) [Brooke, 1996] [Appendix B].

Data analysis Face tracking data (captured through FaceAPI) and game data (task events and player data in RehabCity) were logged into a CSV file and parsed to MATLAB (MathWorks Inc., Massachusetts, US) for later analysis. Face tracking data have been manually cleaned from artifacts and smoothed with a moving average filter (30 seconds window) for cutting-off all high frequencies and noise. Only head orientation data within the field of view of the monitor (±25° horizontal, ±10° vertical) was considered (Figure 3.1).

3.3 Results

Data from 10 training sessions were gathered. Face tracking data were used to measure gaze behavior - based on the face orientation (degrees) - into the four quadrants of the screen. The in-game data of RehabCity includes the overall score, task duration (in seconds), overall distance traveled, position and orientation of the virtual character and all the events within the tasks. This data, combined with the cognitive screening, enables us to quantify the relationship between the in-game data (patient's behaviors within the game), and real-world measurements (gaze behavior, usability, and cognitive evaluation).

3.3.1 System Use

To understand the usage of the on-screen game elements by the study participants we generated a low-resolution gaze heatmap from the FaceAPI data averaged from all patients (Figure 3.4). To simplify the analysis and avoid inaccuracies from the data, we clustered gaze in 4 quadrants. Of those, the top-right quadrant - where the objective list is placed - and the bottom-left quadrant) - where the mini-map for navigation is located – are the most relevant. Data show that throughout the game, the top-right quadrant is the most active one (49% of the time), confirming that users consulted the objective list frequently and relied heavily on it. On the other hand, users did not rely on the RehabCity mini-map (11% of the time). This may suggest that the information provided by the mini-map was redundant with the directional arrow. A Pearson correlation analysis, however, revealed no relationship between the frequency of use of those two quadrants and the performance in the game. Moreover, we found no further correlation with age or computer experience. This indicates that the design of RehabCity can support both computer literate as well as for non-experienced users. Patients reported a high System Usability Scale (SUS) score (M = 77, SD = 14.1), revealing good effectiveness, efficiency and satisfaction levels. However, we found a low correlation between SUS scoring and game performance ($r = 0.64$, $p < 0.05$), indicating that patients that had more difficulty in using RehabCity had also a lower game performance. A further analysis revealed no correlation between SUS scoring and computer experience.

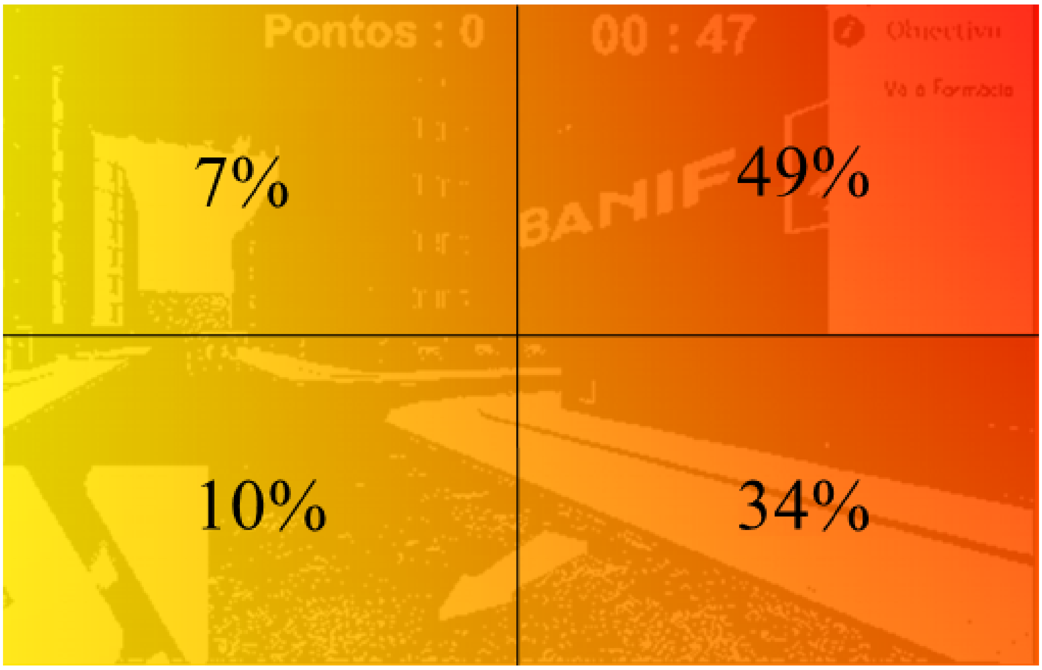


Figure 3.4: Gaze heatmap based on FaceAPI tracking data, clustered in four quadrants.

3.3.2 RehabCity as a Cognitive Assessment Tool

In order to understand how performance in the RehabCity can be used to monitor impairment and track changes during cognitive rehabilitation, we performed a correlation analysis of the in-game data with the demographics and cognitive profiles of patients (Table 3.1). The in-game variables that we considered include score, score progression over time (slope of the linear regression of score vs. time), distance, % of the time in navigation tasks, and % of the time in simulated ADLs. The RehabCity score accumulates the points during the 20 minutes long training session. Based on the reported correlation value, the strongest relationship we find is with the Mini-Mental State Examination (MMSE) test. The MMSE is a well-established clinical instrument that assesses cognitive function in several domains. The high correlation ($r = 81$, $p<0.05$) indicates that the tasks within RehabCity address the cognitive functions as targeted in its design, and supports the idea of using it for cognitive assessment and monitoring tool throughout the rehabilitation process. Further, we also observed a high correlation value ($r=0.75$, $p<0.05$) with mood stability and control, as assessed by the Stroke Impact Scale (SIS). Patients reporting higher mood stability show better performance in the game.

With respect to patient's demographics, we found a negative correlation between score and age ($r = -0.84$, $p < 0.05$), indicating that younger users achieve better scores. We also found a lower but still significant positive correlation with the number of years of schooling ($r = 0.67$, $p < 0.05$). Nonetheless, there was no significant relationship with computer experience. Users reaching higher scores in the game generally visit more ADLs locations, thus covering larger distances (Figure 3.5). However, the overall distance traveled is also related to the efficiency of the navigation task, being a more inefficient navigation in case of longer trajectories. This is supported by a positive correlation of the in-game distance traveled and the MMSE ($r = 65$, $p < 0.05$), showing a similar but weaker relationship of distance with cognitive ability

	MMSE	PC Exp.	SUS	Education	Age	Gender	Task List	Mini-map	Strength	ADL	Communication	Mood	Hand Function	Memory	Mobility	Recovery	Social
Score	0.81*	0.49	0.64*	0.67*	-0.84*	-0.5	-0.34	-0.14	0.2	0.42	0.19	0.75*	0.51	-0.03	-0.39	0.38	0.48
Regression Slope	0.46	-0.2	-0.32	0.2	-0.28	-0.057	-0.15	0.2	-0.37	0.08	0.55	0.46	0.14	0.38	0.13	0.57	0.3
Distance	0.65*	0.46	0.31	0.53	-0.82*	-0.36	-0.33	-0.23	0.34	0.5	0.18	0.46	0.58	-0.01	0.34	0.54	0.54
Nav. Time	-0.57	-0.36	-0.31	-0.78*	0.74*	0.36	0.19	0.3	-0.06	-0.36	-0.51	-0.72*	-0.38	-0.29	-0.36	-0.48	-0.56
ADL Time	0.56	0.35	0.32	0.78*	-0.73*	-0.37	-0.18	-0.3	0.05	0.35	0.5	0.72*	0.37	0.28	0.35	0.47	0.55

*p < 0.05

Table 3.1: Correlation analysis between in-game data (rows) and patient data including (columns). Black boxes indicate a significant correlation (p<0.05) and gray boxes a tendency (p<0.1). See text for further information.

as found with the score. A strong negative relationship of the score with age is also found in the distance traveled (r = -82, p <0.05), meaning that younger patients perform better.

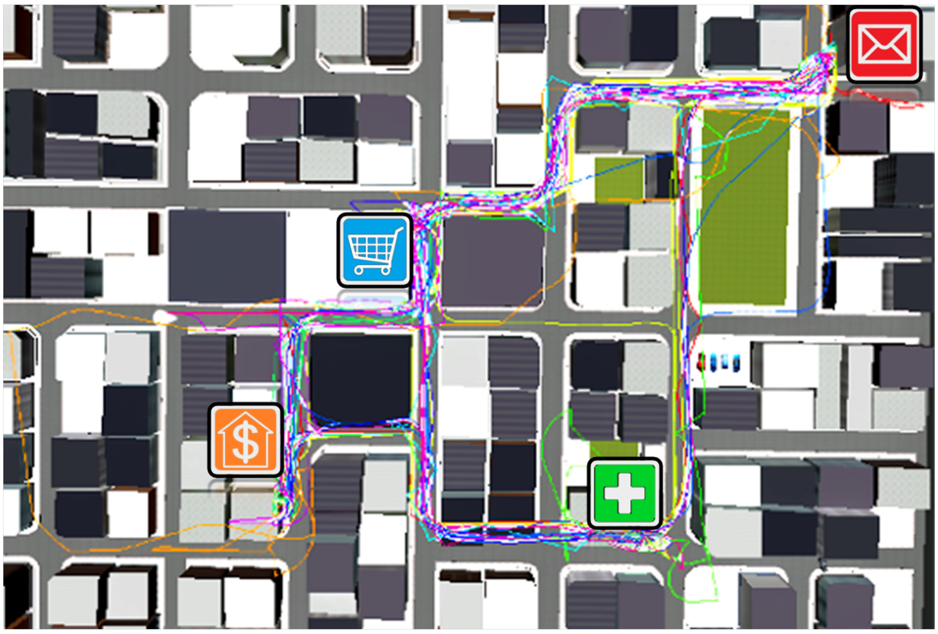


Figure 3.5: RehabCity map displaying the trajectories of the study participants and locations of interest.

The time the player spends in the game is divided between navigation time and time in simulated ADLs. Interestingly, higher education levels in patients contribute towards spending more time performing ADLs (r = 0.78, p<0.05), whereas, age contributes towards older patients spending more time in navigation tasks (r = 0.74, p<0.05). This is mainly due to the automatic progression on the difficulty levels of the game, which makes "better" players face more difficult ADLs challenges. The time spent performing ADLs is also modulated by mood stability (r = 0.72, p<0.05). This trend is also consistent with the reported tendencies in cognitive, MMSE (r = 0.56, p<0.1), and social abilities of the patient (r = 0.55, p<0.1). Finally, we also observed tendencies ($p<0.1$) in the data that suggest a relation between hand function and distance, perceived recovery with progress rate in the game, and social abilities with time spent performing ADLs (See Table 3.1 for the complete correlation analysis).

3.4 Discussion and Conclusion

In this work, we presented the design, implementation and deployment of RehabCity, a novel online game for the rehabilitation of cognitive deficits through a gamified approach on ADLs developed with the RehabNet Framework. We have evaluated the system with 10 stroke patients that reported high usability scores (M=77%) concerning effectiveness, efficiency, and satisfaction. Through the analysis of gaze behavior, we observed that patients relied more on the in-game provided goal list than on the navigation map. We presented a quantitative analysis to validate RehabCity as training, assessment, and monitoring tool, capable of addressing several cognitive domains. This is evidenced by a high correlation between RehabCity scores and the MMSE ($r = 0.81$), being thus the score an appropriate measure to assess the severity of the cognitive impairment. Results show that education level has an effect on score and time (both in navigation and during task performance) in interacting with a computerized system for ADL's and its content. Both the high correlations between cognitive functions and mood stability are consistent with previous studies [Parikh et al., 1987, Kauhanen et al., 1999]. Indeed, the cognitive impairment of individuals with depression has been shown to be consistent with a global-diffuse impairment of brain functions [Veiel, 1997]. To sum up, we found that score is mainly determined by the integrity of cognitive functions, but that other factors that also contribute towards higher scores are years of schooling, lower ages, better mood and emotional stability. Our results contribute towards the understanding of the design process for a complete gamified cognitive assessment and training tool for cognitive rehabilitation that cannot be found so far in the field of virtual rehabilitation. This information can help us move towards Virtual Rehabilitation tools designed for patient profiling, as a tool for automatically personalizing training tasks to cognitive impairment levels and recovery prognosis.

Chapter 4

Using the RehabNet Framework to Study Eye-Gaze Patterns in a VR Rehabilitation Task

A Study with Healthy participants and Stroke Survivors

4.1 Introduction

Prior research [Oztop et al., 2013] has shown that dual activation of mirror neurons during observation/execution is explained by two processes: i) automatic engagement of mental state inference during action observation, and ii) forward prediction by the mirror neurons for motor control during action execution. Furthermore, through neuroimaging techniques, researchers have been able to locate specific areas of brain activation and determine the spatial and temporal congruency between observing and executing actions [Grèzes and Decety, 2001, Holmes et al., 2010]. However, no existing model allows us to fully understand the shared neural mechanisms between observation and execution, and propose how to maximally exploit it in motor rehabilitation training. A promising method for quantifying observation of goal-oriented actions is by measuring eye movements [Liversedge and Findlay, 2000], since eye gaze is linked to sensory prediction during both action observation and action execution [Brouwer et al., 2009]. Studies have demonstrated congruency in gaze metrics between action execution and action observation, supporting the idea that these processes have a partially shared neural network [Causer et al., 2013]. From a rehabilitation standpoint, some studies have demonstrated strong evidence that action observation has a positive effect on rehabilitation of motor deficits after stroke [Ertelt et al., 2007, Mulder, 2007]. Other studies [Loconsole et al., 2011] have shown the feasibility of using eye tracking in neurorehabilitation. With the increasing availability of low-cost devices, eye gaze will play an important role in rehabilitation and diagnostics. In this study we take advantage of the shared neural mechanisms in action observation and execution to explore their potential in rehabilitation. We propose a novel technology that assesses eye gaze behavior in a virtual reality (VR) observation task. We demonstrate its use in healthy subjects as well as in stroke patients, suggesting important implications for diagnostic and rehabilitation purposes.

4.2 Objectives

The objective of this study is to assess eye gaze behavior in a VR observation task in healthy participants and stroke patients. The eye gaze of participants is analyzed in a task where subjects observe an arm in a virtual environment while executing reaching and grasping actions. We aim at verifying the following hypotheses:

(a) Existence of differences in gaze metrics in healthy participants using their dominant arm when compared to their non-dominant arm during action observation, due to interference of arm dominance during the task;

(b) Existence of differences in gaze metrics in healthy participants during normal condition versus simulated impairment condition, while observing the task;

(c) Existence of differences in gaze metrics in stroke patients using their paretic arm when compared to their non-paretic arm during action observation, due to the recruitment of the motor control areas affected by stroke.

4.3 Methods

4.3.1 Participants

For the healthy group, 20 participants (3 female and 17 male) were recruited with a mean age of 30.4 years (SD = 6.5 years). All but one participant were right handed. For the stroke patients group, 10 stroke survivors (5 male, 5 female), with a mean age of 66.1 years (SD = 10.6 years) and a mean of 221.2 days after stroke (SD = 157.4 days), participated in the study. 7 of these patients suffered an ischemic stroke and 3 patients suffered an intra-cerebral hemorrhage. 4 patients had a left-sided brain lesion and 6 patients had a right-sided lesion. Patients with no arm mobility and/or with severe attention deficits were excluded from the study. Stroke patients were recruited from Hospital Dr. Nélio Mendonça and Hospital Dr. João de Almada, located in the city of Funchal, Portugal. Participants in both groups were naive to the system and hypotheses being tested. All of them supplied written informed consent prior to participation. The study was approved by the Ethical Committee of the Regional Health System of Madeira (SESARAM).

4.3.2 System

A custom VR task was developed using the Unity 3D game engine (Unity Technologies, San Francisco, USA). The VR environment was displayed on a 4:3 monitor (1024 x 768 pixels resolution) with an integrated eye tracking system, the Tobii T120 Eye Tracker (Tobii Technology, Stockholm, Sweden). Eye movements were recorded at a sampling rate of 60 Hz. A laptop computer connected to the eye tracker ran the custom VR software during the trials. Eye tracking data were acquired, logged and sent to VR through the Reh@panel.

4.3.3 Procedure

Participants were presented with a simple reach-and-grab and place-and-release task in the virtual environment (see Figure 4.1). The environment was presented in a first-person perspective, allowing the virtual arm to be consistent with the participant's point of view. The task consisted of grabbing a virtual ball (either with a left or right virtual arm), moving it to a target destination (which would make the ball disappear), then come back to the initial position and wait 3 seconds for the task to restart. There were four pre-defined points for the ball's initial position, all equidistant to the target and horizontally symmetric. Both groups were presented with 2 different conditions, in the following order: (i) action observation – the participants were required to observe, for posterior repetition, a pre-recorded execution of the virtual arm grabbing the ball and taking it to the target destination; and (ii) action execution with eye gaze – the participants were required to actively grab the ball with the virtual arm using their eye gaze and to take it to the target destination. In addition, healthy participants had to perform these two conditions twice, in a normal situation and a constrained-induced movement situation. For each condition, each participant had to perform (or observe) 40 repetitions of the task for each arm, with each repetition lasting around 5 s. The order of the initial position of the virtual ball was chosen randomly (out of the 4 predefined positions) for every repetition, making sure that all initial positions were presented 10 times. In this paper we focus on the analysis of condition i). The results of ii), did not show strong correlations with arm motor deficits and thus, are not included in this paper.

4.3.4 Data analysis

All data analysis was performed with MATLAB (MathWorks Inc., Natick, MA, USA). Eye tracking data was temporally smoothed with a Gaussian window of 1.6 seconds with SD = 0.16 s, and converted to screen coordinates (X,Y). Resting periods and segments with missing data were removed from the analysis. According to the velocity profile of the data, eye tracking behavior was classified into 1) fixations, 2) saccadic movements, and 3) smooth pursuit. For each behavior detected, the number of occurrences and their duration were assessed. In addition, the accumulated travelled distance was also computed. Out of the 10 stroke participants, 1 dataset of the action observation condition was corrupt. The 2-sided Lilliefor test revealed that data

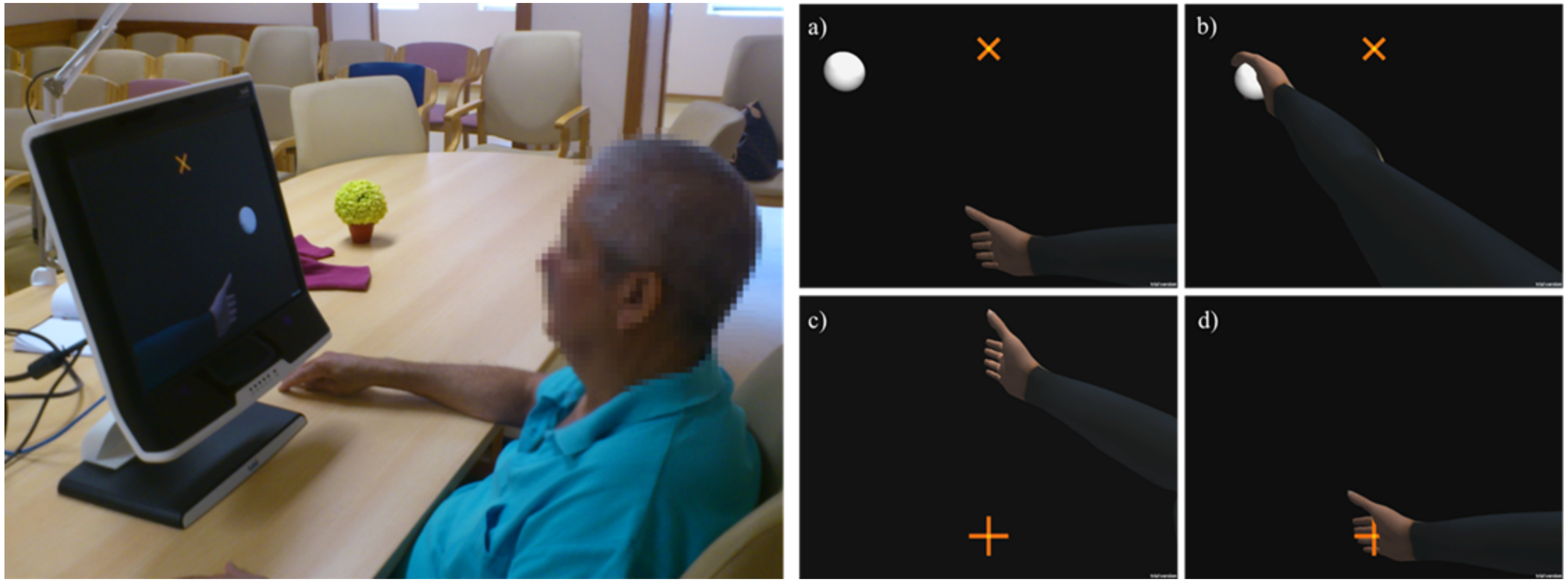


Figure 4.1: Experimental setup being used by a stroke patient, consisting of a monitor with an integrated eye tracker running a custom made VR task. The task consist of 4 steps: a) reaching and grasping of a virtual ball, b) placing it at the target, c) releasing it, and d) moving back to initial position (adapted from:[Alves et al., 2016]).

was not normally distributed. To test against different conditions where size group data differ in size the non-parametric Mann-Whitney test was used. A non-parametric matched pairs Wilkoxon test was used to assess differences between paretic and non-paretic data for the stroke patient data – and to assess differences between dominant and non-dominant data, and between constrained and non-constrained conditions for the healthy participant data.

4.4 Results

4.4.1 Gaze density maps

The distribution of eye gaze patterns (fixations, saccadic movement, and smooth pursuit) in action observation was assessed in the healthy group, for the normal and constrained conditions, and in the stroke patients group (see Figure 4.2).

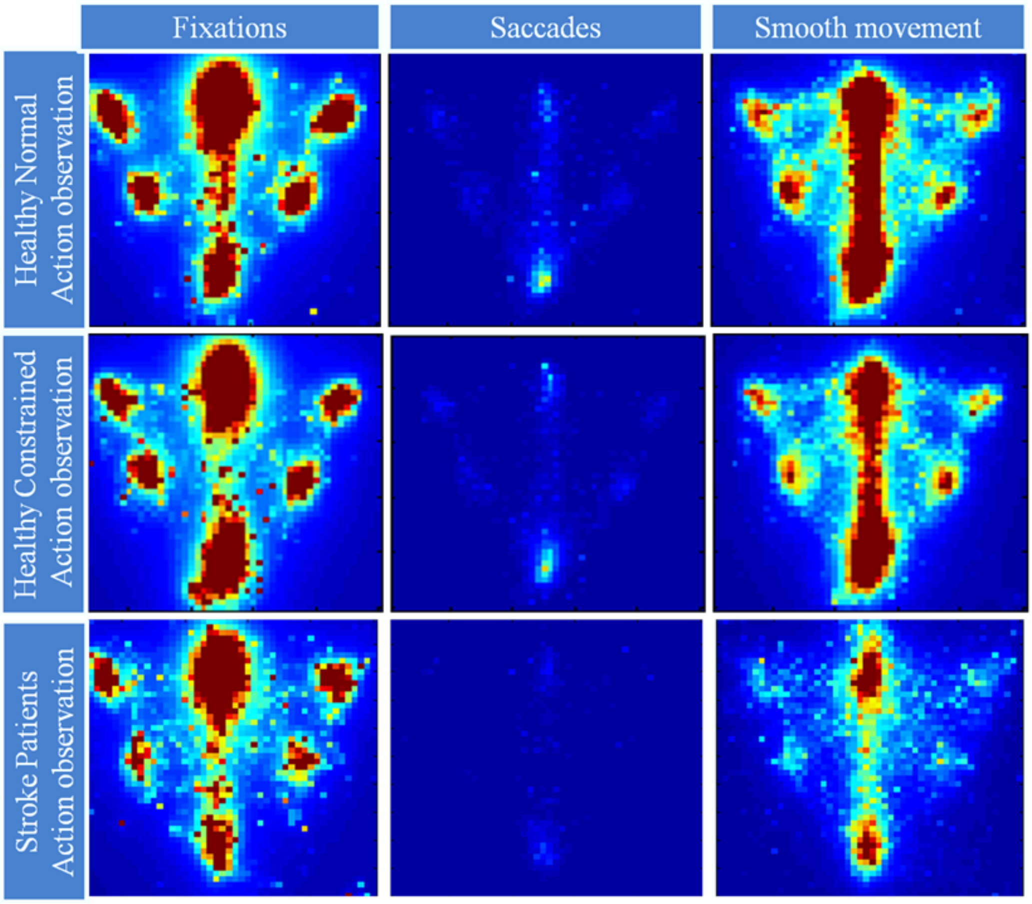


Figure 4.2: Density maps for action observation according to the detected eye movements in the healthy group and stroke patients group (adapted from:[Alves et al., 2016].

There is consistency when we compare eye gaze patterns between the 2 experimental conditions for healthy participants and stroke patients. Fixations are mostly clustered around the targets (release place at the top-center and resting position at the bottom-center of the screen) or virtual objects (2 on the right and 2 on the left halves of the screen) as shown in Figure 4.1. Saccadic movements were detected mostly between the target position and the resting position. Because these two elements are at opposite ends of the screen they generate more saccadic movements. Smooth movements are detected mostly in the areas between virtual objects and their respective targets. We did not observe major differences in the distribution of eye gaze patterns when comparing the different conditions.

4.4.2 Gaze metrics

For the next analysis, the following gaze metrics were extracted from the eye tracking data: number of fixations, number of saccades, number of smooth pursuit segments, duration of fixations, duration of saccades, and duration of smooth pursuit segments (see Table 4.1).

When performing a within subject analysis to the different eye gaze patterns in healthy participants in the normal observation conditions, results revealed shorter saccades when observing the dominant arm (Mdn=265 ms) than when observing the non-dominant arm (Mdn=291 ms), T=31, p¡0.01, and less smooth pursuit events when observing the dominant arm (Mdn=314) compared to the non-dominant arm (Mdn=379), T=37, p¡0.05. No significant differences were found between dominant and non-dominant arm in the movement constrained condition. In the case of stroke patients, the within subject analysis revealed longer smooth pursuit when observing the paretic arm (Mdn=587 ms) than when observing the non-paretic arm (Mdn=567 ms), T=154, p¡0.01. In average, smooth pursuit in the observation condition was 30 ms longer. However, no more differences were found in any other eye gaze metric for stroke patients. When comparing the normal condition and movement constrained condition in the healthy group and with the stroke group, it was found that fixations are less likely to occur in the constrained condition (Mdn=1160) when compared to the normal condition (Mdn=1286), T=224, p¡0.05, and with stroke patients (Mdn=1284),

Table 4.1: Median values of the eye gaze metrics in action observation for each arm, in the healthy group and stroke patients group. (*) indicates significant within condition arm differences. (NC) indicates significant differences between normal and constrained conditions. (NS) indicates significant differences between normal and stroke groups. (CS) indicates significant differences between constrained and stroke groups.

	Healthy Normal			**Healthy Mov. Constrained**			**Stroke Patients**		
	Dom.	**Non-D.**	**Total**	**Dom.**	**Non-D.**	**Total**	**Paretic**	**Non-P.**	**Total**
Fixation count	1309 (NC)	1243	1286 (NC)	1061 (NC)	1261	1160 (NC) (CS)	1295	1272	1284 (CS)
Fixation duration (ms)	234	210 (NC)	228 (NS)	243	174 (NC)	201	384	376	378 (NS)
Saccades count	58	60	60 (NS)	58	59	59	53	52	53 (NS)
Saccades duration (ms)	265 (*)	291 (*)	277	272	275	272	271	276	273
Smooth pursuit count	314 (*)	379 (*)	358	307	320	311	361	403	364
Smooth pursuit duration (ms)	621	577	600	560	604	600	587 (*)	567 (*)	567

U=682, p¡0.01. Additionally, differences in the dominant arm were found between normal (Mdn=1309) and constrained conditions (Mdn=1061), T=34, p¡0.05. The duration of fixations was found to be significantly longer in stroke patients (Mdn= 378 ms) than in the normal condition for healthy participants (Mdn=228 ms), U=696, p¡0.01. Differences were also found for the non-dominant arm between normal (Mdn=210 ms) and constrained conditions (Mdn=174 ms), T=28, p¡0.01. Finally, less saccades were detected for stroke patients (Mdn=53) than for healthy participants in the normal condition (Mdn=60), U=370, p¡0.05. No other significant differences were found between conditions and groups.

4.5 Conclusions

There is a growing body of research that supports the use of action observation as a valid paradigm for post-stroke rehabilitation due to shared neural mechanisms between execution and observation circuits. In this study we quantified action observation metrics, by means of the combination of VR and eye tracking technology, showing its correlation to execution deficits.

Differences in gaze metrics were found when comparing normal condition with simulated impairment in fixation count and duration, and with stroke patients in fixation duration and saccades count. Movement constrained condition data and stroke patients were consistent in fixation duration, saccades count. Saccades duration, smooth pursuit count and duration were not modulated by the conditions. However, a handedness effect was detected in the normal condition (saccades duration and smooth pursuit count) and differences between paretic and non-paretic arms were detected in stroke patients (smooth pursuit duration). Hence, data suggests that gaze metrics are differently sensitive to motor impairment, stroke and handedness. This fact supports the results found in stroke patients, by showing that differences between the paretic and non-paretic arms in the observation condition (differences in smooth pursuit duration) could not be due to arm dominance or movement constrain, but to some other factor such as the recruitment of motor control areas of the brain affected by stroke.

Consequently, considering the first hypothesis (a), we found differences between dominant versus non-dominant arm only during action observation. Consistent with the second hypothesis (b), the differences shown between the constrained and non-constrained condition demonstrate that simulating the motor limitations of post-stroke patients in healthy participants also affects their eye gaze during observation of a goal-oriented task, and some of them consistent with stroke data. Considering hypothesis (c), differences were found between paretic and non-paretic arm during action observation, which may be explained by the recruitment of motor control areas of the brain affected by stroke. Consequently, with the increasing appearance of low-cost eye-tracking devices, treatments aiming at exploiting the shared mechanisms between eye gaze control and action observation can become a cost-effective continuous assessment and rehabilitation tool for at home use after hospital discharge. The findings of this study strongly suggest that eye tracking combined with an action observation task can be used to assess motor deficits derived from stroke, and therefore has a large potential to be used in its motor rehabilitation.

Virtual Rehabilitation Summary

So far, we observed the impact of the interface dimensionality in training (2D vs 3D setup), but also the difference between pen-and-paper vs VR. Current results showed improvements and emphasize the value of rehabilitation approaches which combine cognitive and motor training, highlighting the interface contribution on each domain.

Furthermore, the impact of cognitive and motor deficit to the performance of the activities of daily living was observed at the pilot assessment of virtual scenarios of every-day life through Rehabcity. In addition, we highlighted the impact of hand dominance, hand constraint level, and lesion side at the Eye-Gaze Patterns during an action observation VR Rehabilitation Task.

While current results illustrated the potential of the RehabNet framework, the inclusion criteria could not involve patients with high levels of spasticity and low motor capability due to optical hand tracking. We, therefore, extended the RehabNet platform by developing neurofeedback tools for training, enhancing the capabilities of the system for involving the excluded patients.

Part III

Neurofeedback

Optimizing Motor-Imagery based Brain-Computer Interaction

Introduction

For including patients with low or no active movement, the idea of utilizing Brain-Computer Interfaces (BCIs), was fostered in order to complement current VR rehabilitation strategies [Bermúdez i Badia and Cameirão, 2012, Lange et al., 2012]. To date, patients with low level of motor control –such as those suffering of flaccidity or increased levels of spasticity [Trompetto et al., 2014]- could not benefit due to low range of motion, pain, fatigue, etc (see Figure 4.3). Figure adapted from video footage[1].

[1]`https://www.youtube.com/watch?v=A_F8naalfEo`

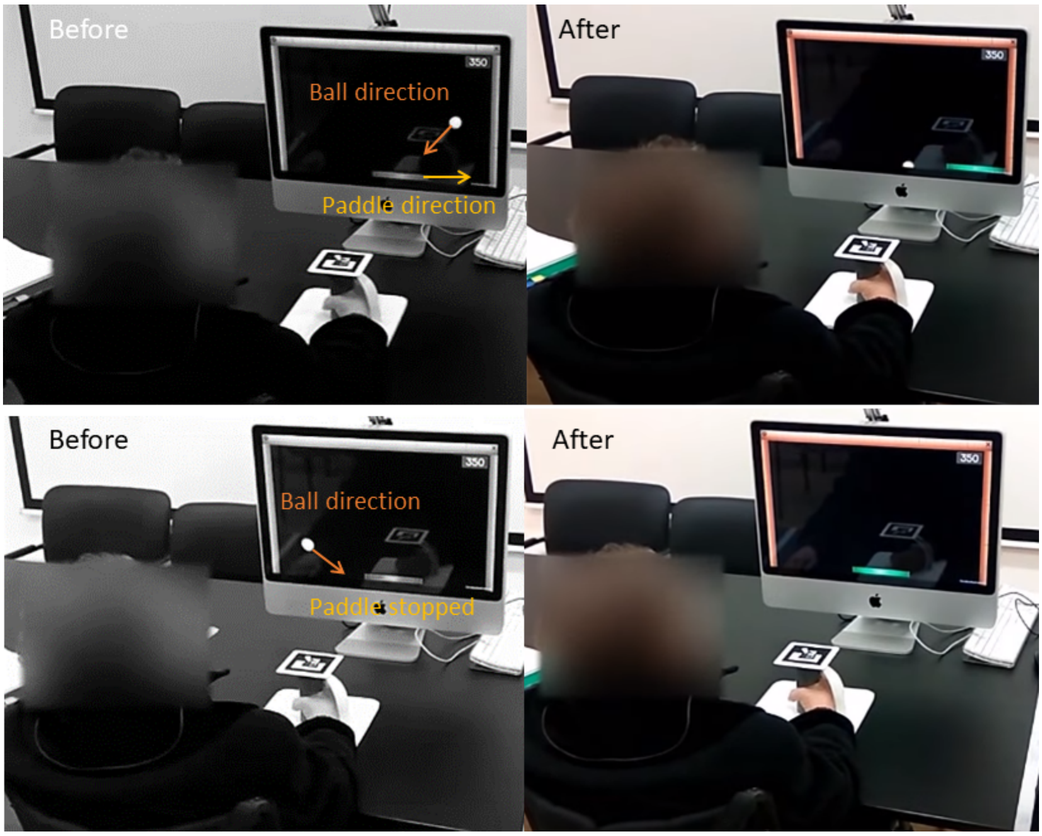


Figure 4.3: Example of a low-mobility stroke patient (Fugl Meyer: 26/66, Motricity index: 51/100) undergoing virtual rehabilitation motor training using a grasping object together with camera tracking for interacting with the game.

Virtual Reality (VR) feedback in MI BCI training is offering a more compelling experience to the user through 3D virtual environments [Lotte et al., 2013a]. The fusion of BCI and VR (BCI-VR) allows a wide range of experiences where participants can control various aspects of their environment -either in an explicit or implicit manner-, by using mental imagery alone [Friedman, 2015]. This direct brain-to-VR communication can induce illusions mostly relying on the sensorimotor contingencies between perception and action [Slater, 2009].

Motor Imagery (MI) is the mental rehearsal of movement -without any muscle activation- and is a mental ability strongly related to the body or 'embodied' cognition [Hanakawa, 2015]. MI appears to largely share the control mechanisms and neural substrates of actual movement both in action execution and action observation [Eaves et al., 2014], providing a unique opportunity to study neural control of movement in either healthy people or patients [Mulder, 2007, Neuper et al., 2009]. Since MI leads to the activation of overlapping brain areas with actual movement, and because sensory and motor cortices can dynamically reorganize [Lledo et al., 2006, Rossini et al., 2003], MI constitutes an important component for motor learning and recovery, therefore, MI has important benefits through its utilization as a technique in rehabilitation for people with neurological impairments [Dickstein et al., 2013]. MI offers an important basis for the development of brain-to-computer communication systems called Brain-Computer Interfaces (BCIs). BCIs are capable of establishing an alternative pathway between the brain and a computer or prosthetic devices [Wolpaw et al., 2002] that could assist (assistive BCI) or rehabilitate physically (restorative BCI) disabled people and stroke survivors [Dobkin, 2007].

In the following chapters, results from motor-imagery based brain-computer interfaces (MI-BCIs) are illustrated in an attempt to optimize current MI-BCI paradigms for rehabilitative use. As a first step, different EEG systems had been assessed for their cost-effectiveness, in order to be utilized through the RehabNet framework, broadening accessibility [Vourvopoulos and Bermudez I Badia, 2016]. Next, we assess the role of motor-priming in a BCI-VR paradigm [Vourvopoulos and Bermúdez i Badia, 2016] as-well-as the user profile and prior gaming experience [Vourvopoulos et al., 2016a] in order to maximize BCI performance of first-time users. Finally, a complete BCI-VR environment for MI training is introduced which makes use of multimodal feedback through an immersive Head Mounted Display [Vourvopoulos et al., 2016b] and initial results of an adaptive performance engine for enhancing BCI control [Ferreira et al., 2015].

*Parts of the content of this chapter were published at:

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- ***Vourvopoulos, A.***, *& Bermúdez i Badia, S. (2016). Motor priming in virtual reality can augment motor-imagery training efficacy in restorative brain-computer interaction: a within-subject analysis. Journal of NeuroEngineering and Rehabilitation, 13(1), 1–14.*
- ***Vourvopoulos, A.***, *Bermúdez i Badia, S., Liarokapis, F., (2016). EEG correlates of video game experience and user profile in motor-imagery-based brain-computer interaction. The Visual Computer 33(4): 533-546 (2017)*
- * ***Vourvopoulos, A.***, *Ferreira, A., Bermúdez i Badia, S. (2016). NeuRow: An Immersive VR Environment for Motor-Imagery Training with the Use of Brain-Computer Interfaces and Vibrotactile Feedback. Presented at the PhyCS 2016 - 3rd International Conference on Physiological Computing Syst, Lisbon.*
- *Ferreira, A.,* ***Vourvopoulos, A.***, *& Bermudez I Badia, S. (2015). Optimizing Performance of Non-Expert Users in Brain-Computer Interaction by Means of an Adaptive Performance Engine. In Lecture Notes in Computer Science/Artificial Intelligence (LNCS/LNAI). London, UK: Springer.*

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Chapter 5

Usability and Cost-effectiveness of Low-Cost Systems in Brain-Computer Interaction

5.1 Introduction

In the last few years, low-cost commercial EEG devices and Open Source projects[1][2], are offered as alternatives to expensive medical equipment. However, results are mixed and it is not clear if they can deliver comparable user experiences as compared to medical-grade EEG systems. In a recent study, it was investigated the difference in comfort between the Emotiv EPOC headset and silver chloride scalp discs in a P300 paradigm [Nijboer et al., 2015]. It was found that the Emotiv EPOC was more uncomfortable than the attached disks and discomfort increased over time. Another comparative study between the Emotiv EPOC and a medical grade headset in a P300 paradigm

[1] `http://openbci.com/`

[2] `http://openeeg.sourceforge.net/doc/`

reported that the Emotiv was better in terms of price, setup process, and intrusiveness. On the other hand, the ANT system was reported to be more comfortable, cheaper to maintain and more durable [Duvinage et al., 2013]. A usability comparison between four commercially oriented EEG systems: B-Alert, Emotiv EPOC, Biosemi's ActiveTwo and QUASAR's Dry Sensor Interface, revealed that overall in (i) the adaptability for different head sizes, (ii) comfort and preference, (iii) variance for the recording scalp locations for the recording electrodes , (iv) the stability of the electrical connection and (v) the integration between the EEG system and stimulus presentation, participants preferred the B-Alert system [David Hairston et al., 2014]. In MI, a new comparative study between the Emotiv EPOC and the Biosemi ActiveTwo system showed that performance is comparable between the same number of sensors and sensor positions for a three-class MI [Martinez-Leon et al., 2016]. Many studies have investigated the usability of BCI applications as a whole. Nijboer et al investigated the acquisition component and compared the usability of three different EEG headsets (Biosemi, Emotiv EPOC, and g.Sahara) in a P300-paradigm including also classification score information [Nijboer et al., 2015]. Overall, most of the comparative studies have used the P300 paradigm but similar information between different headsets in SSVEP or MI is limited.

MI-BCI training is based on visuomotor imagination and together with other mental task imagination (e.g. mental subtraction, word association) [Friedrich et al., 2012] is the only paradigm of endogenous nature that does not require external stimulation but only the user's imaginative action. In addition, MI is considered the most important type of BCI paradigm for motor function restoration. Results from previous studies have proven mental practice of action to be useful in MI-BCI [Prasad et al., 2010], and have shown beneficial effects of motor imagery practice during stroke recovery [Pichiorri et al., 2015]. Unfortunately, an estimated 15-30% of people cannot use a BCI system, resulting in a big amount of BCI illiteracy in the user base [Vidaurre and Blankertz, 2010]. In this study, our main focus is on the MI-BCI paradigm because it is self-paced, and also because of its utilization in rehabilitation. Our hypothesis is that brain-computer interaction throughput in non-expert users is not technology related but user related and it can be accomplished without requiring such high-end and high-cost devices. If correct, these findings would support the use of lower-cost approaches for MI-based motor rehabilitation.

To this end we performed a (1) usability assessment following the same protocol as a previous study using the P300 paradigm [Nijboer et al., 2015] in order to have comparable results, and (2) by performing a cost-effectiveness analysis of all tested EEG systems from both BCI studies, in two different paradigms (P300 and MI). For that purpose, a pilot study with 8 non-expert participants using 3 different EEG systems, ranging from an open-source project, commercial system for gaming, to medical certified systems, and a total of 24 BCI training sessions, was conducted.

5.2 Methodology

5.2.1 Participants

8 users (mean age of 29 $\pm$ 4.9 years old, all male) were recruited as a voluntary sample, based on their motivation to participate in the study. All participants were right-handed with no previous known neurological disorder, nor previous experience in BCIs. All participants were University students and academic staff. Finally, all participants provided their written informed consent before

participating in the user study.

5.2.2 Experimental Design

The experiment followed a within-subject design, with each participant taking part in overall three BCI training sessions, one per day, by using a different headset on each session in a randomized order. Before the first session, informed consent was obtained and demographical information was collected. At the beginning of each session, a BCI headset was applied by the experimenters, who logged the time (in minutes) it took from the conductive gel application to the moment that good EEG signals were achieved. Participants then were asked about their perceived setup time (in minutes) and to answer a set of usability questions before starting the experiment.

5.2.3 Experimental Setup

The experimental setup was composed by a desktop computer (OS: Windows 8.1, CPU: Intel® Core™ i5-4440 at 3.3 GHz, RAM: 8GB DDR3 1600MHZ, Graphics: Nvidia GT 630 1GB GDDR3), running the BCI training task. In addition, the Vuzix iWear VR920 (Vuzix, NY, USA) head-mounted display (HMD) was used by the participants in order to focus their attention on the training and prevent any external visual stimulation from the environment. The HMD is made of two 640x480 twin LCD displays, 32-degree field of view (FOV), 3/4" eye relief and 5/16" eye box. The BCI set up comprised of 3 EEG systems. The spatial distribution of the electrodes followed the 10-20 system configuration [Klem et al., 1999] with the following electrodes over the somatosensory and motor areas: Frontal-Central (FC5, FC6), Central (C1, C2, C3, C4), and Central-Parietal (CP5, CP6) as illustrated in Figure 5.1. All three headsets connected via Bluetooth to the desktop computer for the EEG signal acquisition. Data filtering and classification was performed through the OpenVibe platform [Renard et al., 2010]. The Reh@panel [Vourvopoulos et al., 2013] software was used to mediate between the openBCI system and OpenVibe via the Lab Streaming Layer protocol (LSL). For all EEG data, a Common Spatial Patterns (CSP) filter was used, and the classification of motor-imagery actions from the extracted EEG features was determined through a Linear Discriminant Analysis (LDA).

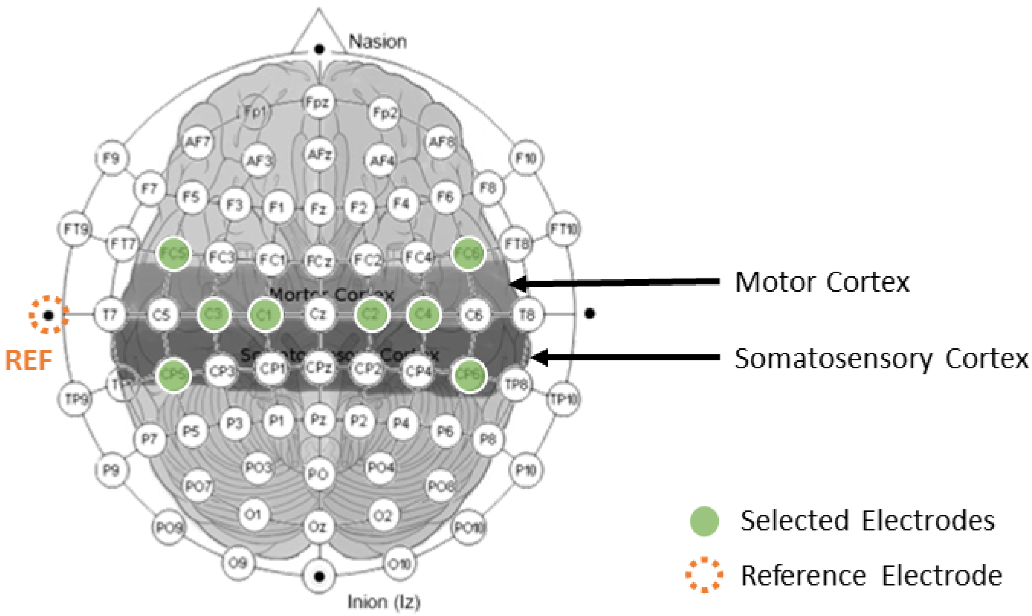

Figure 5.1: Electrode configuration used for the experiment based on the 10-20 system. Electrodes are placed over the motor and somatosensory cortices and reference electrode at the left ear lobe.

Open Source System: The Open-Source BCI system (see Figure 5.2a) is based on the ADS1299 Analog-to-Digital Converter (ADC) developed by Texas Instruments (TI, Dallas, Texas, United States)[3]. This system provides 8 EEG channels operating at sample rates between 250 and 16000 Hz, with a

[3] `http://www.ti.com/product/ADS1299/description`

resolution of 24 bits per channel. The current prototype operated at 250 Hz. An ATmega328 Arduino UNO board was used to sample the ADC board, and for data transmission based on the first OpenBCI V1 data format. The cost for all components and electrodes for the complete system is calculated at 211 euro including VAT.

Enobio 8: Enobio (Neuroelectrics, Barcelona, Spain) is a wearable, wireless EEG sensor with 8 EEG channels and a triaxial accelerometer, for the recording and visualization of 24 bit EEG data at 500 Hz (see Figure 5.2b). Enobio is a CE medically certified product and it is currently classified as an investigational device under US federal law[4]. The cost of the system including VAT is calculated at 6150 euro.

g.MOBIlab+: The g.MOBIlab+ biosignal amplifier (g.tec, Graz, Austria) is a wireless EEG system, composed of 8 active EEG electrodes (see Figure 5.2c) equipped with a low-noise bio-signals amplifier and a 16-bit A/D converter at 256 Hz[5]. The cost including VAT is estimated at 9696 euro.

[4] `http://www.neuroelectrics.com/products/enobio/enobio-8/`

[5] `http://www.gtec.at/Products/Hardware-and-Accessories/g.MOBIlab-Specs-Features`

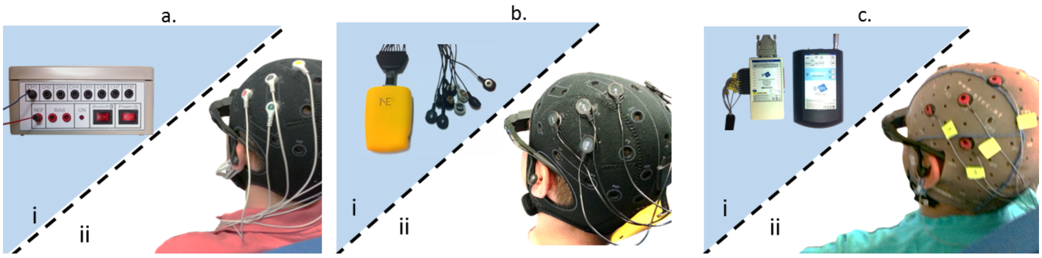

Figure 5.2: From left to right, the openBCI system (a.i) with snap-on type of electrodes using a neoprene cap (a,ii), the Enobio system (b.i) attached in the back of a neoprene cap (b.ii), and the gMOBIlab+ system (c.i) with active electrodes (c.ii).

5.2.4 BCI Training

The BCI training was based on the Graz-BCI paradigm [Pfurtscheller et al., 2003] with directional arrows feedback (see Figure 5.3). When an arrow appears on the screen, the user has to perform a mental rehearsal of a motor task such as grasping, throwing or waving with the corresponding hand. The action selected for mental imagery needs to be sustained during the whole duration of the training session in order to train a linear classifier to distinguish successfully left from right-hand imagery. Each participant went through 3 complete training sessions followed by 3 online sessions (1 set per day for each headset) within one week. On each session, the participant had to perform 20 repetitions per class (left or right) of a 30 seconds baseline measurement followed by cue based motor-imagery training. The cue duration (using a unidirectional arrow) lasted for 4 seconds and was followed by a 1.5-second pause. After the completion of the training session, a 5-minute rest was followed by an online MI-BCI session with the trained classifier. The classification performance of the offline session quantifies the ability of the classifier to distinguish the two classes (left and right-hand imaginary) with cross-validation -based error estimation. In the online session, the classifier needs to identify the two classes from a new stream of data that is acquired online by the user when trying to perform mental imagery within a specific time window. Finally, for all 3 sessions, from 8 participants, 24 EEG datasets were gathered and analyzed.

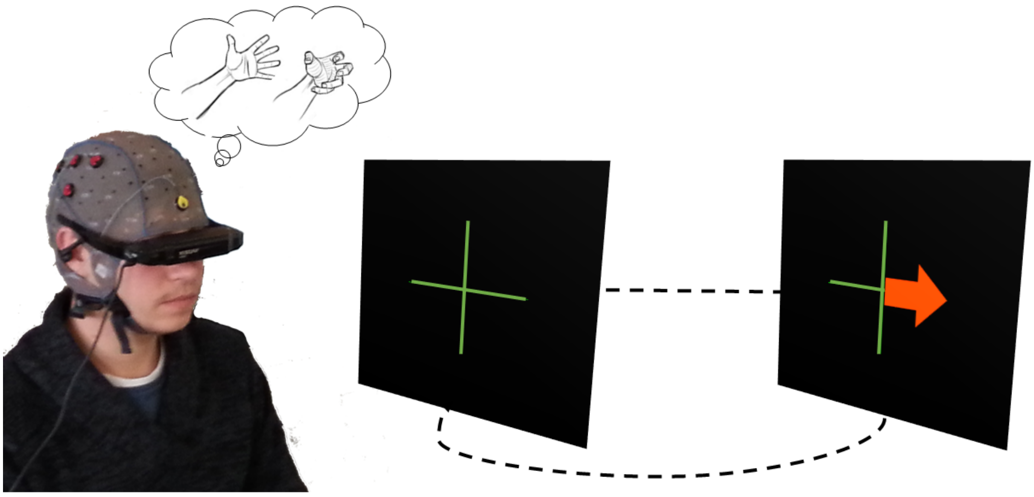

Figure 5.3: Graz paradigm for motor-imagery training. A fixation cross followed by a directional arrow for left or right hand imagery.

5.2.5 Questionnaires

Prior to the BCI training session, demographic data of the participants were collected together with a handedness assessment through the Edinburgh inventory [Oldfield, 1971]. After each setup, participants completed a usability questionnaire (used in a similar usability study [Nijboer et al., 2015]) for comparison. On this questionnaire, participants were asked to estimate the number of minutes it took for the headset to be set up (from the moment of electrode placement until the decision of the experimenter that signals were good). Then, they proceeded to rate on a 7-point Likert scale the 'speed of setup' (1 = very fast, 7 = very slow), level of 'comfort' of the headset (1 = very comfortable, 7 = very uncomfortable), and 'ease of setup' (1 = very easy, 7 = very difficult). Finally, the NASA Task Load Index (TLX) questionnaire [Hart, 2006] was used after each session in order to assess the perceived workload to use each EEG headset in terms of Mental Demand, Temporal Demand, Physical Demand, Performance, Effort and Frustration in a Likert scale with 21 points (1 = very low, 21 = very high).

5.3 Results

In this study, effectiveness was measured in terms of performance - as objectively assessed by the classification accuracy during motor imagery task - and subjectively through the reported workload and the usability reports.

5.3.1 Performance

Classification Performance was computed as the success rate of the correct recognized classes of the training data and also the classifier performance during online task with the use of new data. Mean classification accuracy across participants and conditions was used for statistical analysis through a repeated measure ANOVA since the data was normally distributed as indicated by the Shapiro-Wilk Test.

In terms of training, a statistically significant difference was found between the different headsets from the training data ($F(1.370, 9.590) = 21.112$, $p < 0.005$). Post hoc tests using the Bonferroni correction revealed that openBCI ($M = 56.2$, $SD = 2.3$) performed significantly worse ($p < 0.05$) than Enobio ($M = 67.8$, $SD = 3.4$) and g.tec ($M = 65.6$, $SD = 4.8$) (Figure 5.4a). Enobio and g.tec had no significant differences.

In terms of task performance, we observed that the classifier with the new data acquired during the online task dropped for all headsets. We found no statistically significant main effect of BCI headset in performance ($F(1.997, 13.980) = 16.695$, $p = 0.563$). The highest mean performance was achieved by the g.MOBIlab+ system (M = 51.9 %, SD = 4.2%), followed by the openBCI system (M = 50.5%, SD = 4%), and finally the Enobio system (M = 49%, with the highest data variability SD = 6.6%) (Figure 5.4b).

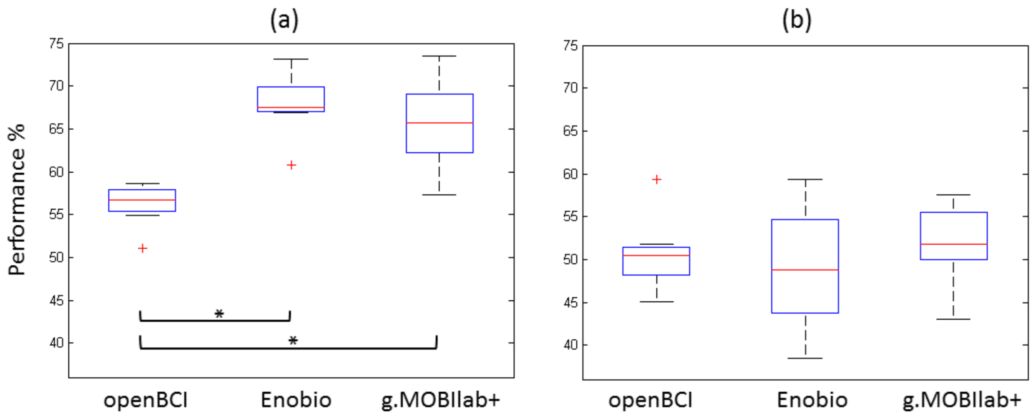

Figure 5.4: LDA classification performance. (a) Classification score between the two classes from the training data, (b) classification score of the two classes from a new dataset during the online session.

5.3.2 Workload

To assess how different headset technology may affect the perceived task workload required to perform the MI task we used the reports from the TLX questionnaire. We found again no significant main effect between the three conditions ($F(1.679, 11.756) = 0.694$, $p = 0.495$), nor in overall workload score as derived from the weighted sum of the TLX domains (Mental Demand, Temporal Demand, Physical Demand, Performance, Effort and

Frustration). Nevertheless, the openBCI system had the highest score in Temporal Demand (M = 8.8, SD = 4.7), Performance (M = 11, SD = 3.2) and Frustration (M = 8.4, SD = 5). Enobio scored the highest in Mental (M = 12.7, SD = 3.7) and Physical Demand (M = 6.7, SD = 2.9). Finally, g.MOBIlab+ scored the highest in Effort (M = 12.5, SD = 2.8) (Figure 5.5).

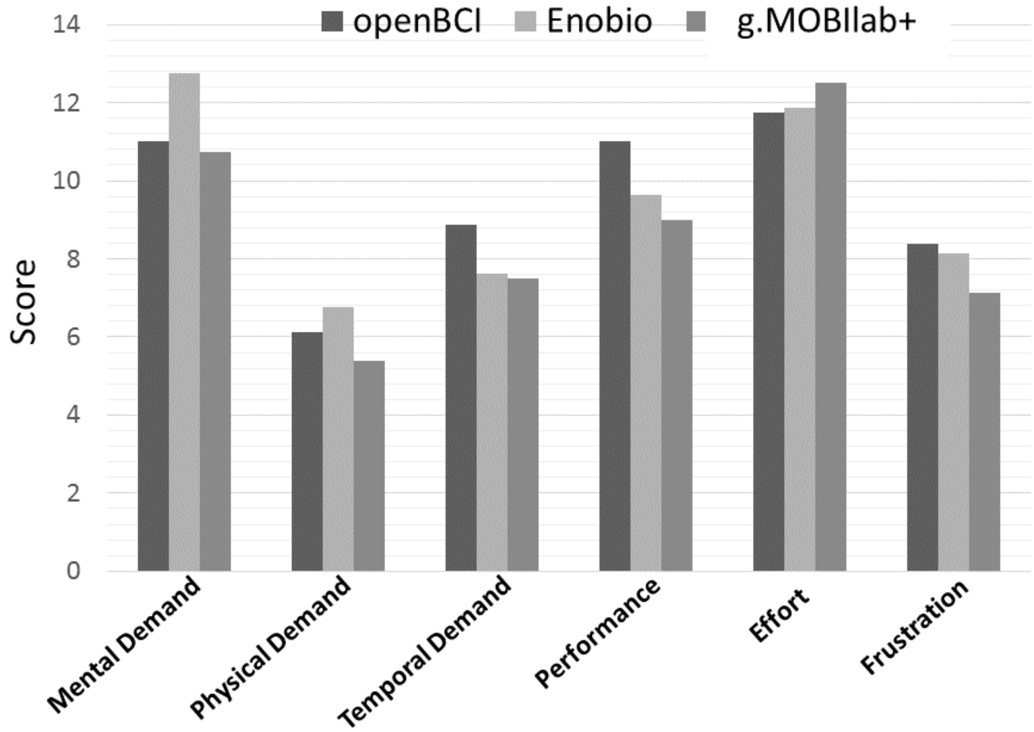

Figure 5.5: Sub-components of the NASA TLX questionnaire for obtaining task workload.

5.3.3 Usability

Friedman's analysis showed no significant effect of the type of headset in any of the usability questions (see Table 5.1). The scores obtained were the following: for speed of setup (1-7) the mean value was M = 5, for all headsets;

for ease of setup (1-7) Enobio and g.tec scored higher (M = 6) than openBCI (M = 5); for comfort (1-7), g.MOBIlab+ was the highest (M = 6) over the other two (M = 5). Finally, on appearance (1-10), g. MOBIlab+ scored the lowest (M = 3) and openBCI and Enobio had a higher score (M = 6) (see Table 5.1 a).

5.3.4 Cost-Effectiveness Analysis

The concept of cost-effectiveness is used in medical decision making and can be illustrated graphically on the cost-effectiveness (CE) plane [Black, 1990]. The CE plane provides a geometrical interpretation of relative cost-effectiveness in terms of their assessed performance (see Figure 5.6). Typically, one or more new strategies are compared against an existing standard. Since there is no standard available for EEG systems, a within system comparison was performed with available data from the literature and the current study. One can visualize the results of such comparisons in CE plane (see Figure 5.6) in which both the MI and P300 effectiveness over cost is represented. For the sake of comparison, we only considered the offline classification score from our study to match the available data from the previously mentioned P300 study [Nijboer et al., 2015]. Additionally, we estimated the cost of the devices reported in that study through online search. From the calculation of the cost-effectiveness ratios (CER) we found that the openBCI system was ranked first with the lowest CER (CER = 3.76), followed by Emotiv (CER = 6.48), Enobio (CER = 90.65), g.MOBIlab (CER = 147.83). The g.Sahara (CER = 159.49) and the Biosemi system (CER = 237.29) score the highest, CER ratio. A repeated measures ANOVA with a Greenhouse-Geisser correction determined that mean CER differed statistically significantly between different BCI systems in both training ($F(1.209, 8.462) = 742.410$, p ¡ 0.001)

Table 5.1: Overview of the usability scores and classification accuracy during training from literature with P300 data (a) using the Biosemi, Emotiv and g.Sahara systems and from this study (b) with openBCI, Enobio and g.MOBIlab.

	(a)			(b)		
	Biosemi (32 channel)	**Emotiv (14 channel)**	**g.Sahara (8 channels)**	**openBCI (8 channel)**	**Enobio (8 channel)**	**g.MOBIlab (8 channel)**
Classification Accuracy	88.5%,(± 18.3)	61.7% (± 25.7)	62.7% (± 37.7)	56.2 (± 2.3)	67.8,(± 3.4)	65.6,(± 4.8)
Real time to setup	20.3 min (± 6.7)	6.9,min (± 3.3)	12.1 min (± 2.9)	6.7,min (± 2.4)	6.1,min (± 1)	4.8,min (± 0.6)
Participant's estimation of time of setup	14.4min (± 5.2)	6.4min (± 4.7)	9.7 min (± 2.9)	6.4 min (± 2.3)	5min (± 1.5)	5.6min (± 1.9)
Speed of setup	4	2	4	5	5	5
Ease of setup	6	3	3	5	6	6
Comfort	3	4	3	5	5	6
Appearance	6	6	4	6	6	3

and online (F(1.779, 12.456) = 339.260, $p < 0.001$). Post hoc tests using the Bonferroni correction revealed that the openBCI system was statistically significantly better from Enobio and gMOBIlab+ systems as well as Enobio from gMOBIlab+.

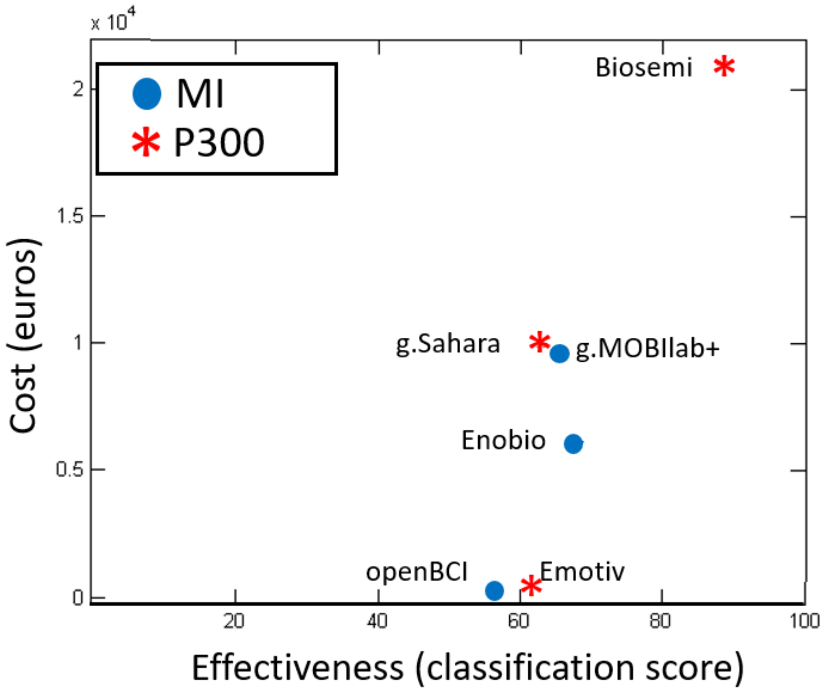

Figure 5.6: CE plane for cost (0-21000 euro) and effectiveness (1-100) for the offline classification on both studies. Systems that locate themselves further or closer from the origin (0,0) if they are more or less effective, and above or below the origin if they are more or less costly.

5.4 Discussion

From the technology side, the effect of intrinsic variability, low signal-to-noise ratio and non-stationarities of EEG signals [Lopes Da Silva, 1978] may explain the low classification accuracies obtained during task performance.

From a user perspective, one of the biggest challenges in BCI research is to understand and solve the problem of "BCI Illiteracy" that is affecting an estimated 15 to 30% of the users [Vidaurre and Blankertz, 2010]. Current limitations are based on the inability of many users to voluntarily modulate the amplitude of the sensory-motor rhythm in order to control the feedback application. Unfortunately, comparisons across different studies have been problematic since different groups use different performance thresholds [Allison and Neuper, 2010]. To date, and to the best of our knowledge, there are no similar studies that investigate the ratio of cost effectiveness, a subjective measure through user experience, and an objective measure which is the classification score. From our current data, we can distinguish a trend in different dimensions concerning the classification performance, perceived workload, usability and cost-efficiency. From the P300 classification (Table 5.1 a), we can distinguish greater standard deviations compared with MI and also lower scores in usability. Unfortunately, the small sample from both studies result in a low statistical power that may prevent capturing some effects. Nevertheless, the fusion of two studies, involving two BCI paradigms is an important step towards understanding the technology transfer and acceptance of BCIs from non-expert users.

5.5 Conclusion

So far, we found significant differences in offline training but no significant differences in the online performance among the 3 EEG headsets from the set of data derived from both subjective sources - through the questionnaires - as well as objective data - derived from the online performance. Given the current findings, devices seem to have similar effectiveness and we can conclude that there is no perceived difference in terms of comfort, appearance, speed/ease of setup and overall workload in the actual system performance. Hence, the low-cost openBCI open source system is the more cost-effective BCI solution as compared with its commercial medical grade counterparts. The comparison in the P300 study [Nijboer et al., 2015] considered different electrode configurations across systems, and a different interaction paradigm (P300 vs MI). Although we cannot directly compare classification scores, we observed that regardless of the BCI paradigm, usability and CER analysis indicate that medical grade and more expensive systems do not necessarily add value on the experience level of the users. Therefore, we can conclude that brain-computer interaction performance/throughput, at least for the particular case of non-expert users, is not technology related and it can be accomplished without requiring high-end and high-cost devices. Current results provide useful pointers towards leveraging research of Brain-Computer Interaction for non-expert users and minimizing BCI illiteracy.

Chapter 6

Understanding the Role of User-Profile and Experience in MI-based BCI Interaction

6.1 Introduction

To date, it has been shown that users regularly exposed to video-games have improved over time their visual and spatial attention, memory, mental rotation abilities [Green and Bavelier, 2003, Feng et al., 2007] and enhanced sensorimotor learning, enabling better performance in tasks with consistent and predictable structure [Gozli et al., 2014]. Extensive video-game practice improves the efficiency of movement control brain networks and visuomotor skills of the users [Granek et al., 2010]. However, there is a limited understanding of how these factors affect the activity patterns of motor-related areas during a motor-imagery task. Since these type of skills are used in current mental tasks used to control a BCI (e.g., mental rotation of geometric figures, motor-imagery, remembering familiar faces [Friedrich et al., 2013]), this suggests that users might improve their mastery of BCI by performing training tasks that do not involve the BCI system. This includes playing various video-games and improving in an indirect way their visuo-motor capabilities. So far, the relationship between video-game practice, player profile and BCI performance have been observed for BCI based on Steady-State Visual Evoked Potentials (SSVEP) [Allison et al.,] but not in MI and still there is currently no available literature to support this hypothesis [Lotte et al., 2013b]. Having BCI users practicing video-games might be a promising indirect training method to improve their BCI control skills and minimize the overall training time. The aim of this paper was to examine the effect that gaming experience has on brain pattern modulation capacity during motor-imagery training to identify the elements that contribute to high BCI control. Our hypothesis is that experienced gamers could have better performance in MI-BCI training due to enhanced sensorimotor learning derived from gaming [Vourvopoulos et al., 2015b]. An experimental study with 20 participants, undergoing MI-BCI training and followed by online control through abstract feedback (Graz BCI paradigm) [Kalcher et al., 1996] was performed. Overall, this research attempted to identify traits in the user profile and if enhanced sensorimotor capability of experienced gamers can be reflected in MI-BCI performance and influence EEG rhythms activation. For this, an experimental setup for assessing the following hypotheses was designed:

1. Examine if the player profile can influence EEG rhythms activity patterns during a motor-imagery task

2. Assess the relationship between video-game practice and player profile with BCI performance.

6.2 Methods

6.2.1 Experimental Design

This experiment is divided into two parts. In the first part, a between-subject design was used for the comparison of two different groups and in the second part a within-subject design but over different sessions. The training protocol of the BCI sessions was the same across both parts of the study and amongst all sessions. In the first part of the study, only one BCI session took place and in the second part, a subset of users performed an additional 2 BCI sessions, one session per day, completing all BCI sessions in 3 days. The setup was composed of a desktop computer (OS: Windows 8.1, CPU: Intel® Core™ i5-4440 at 3.3 GHz, RAM: 8GB DDR3 1600MHZ, Graphics: Nvidia GT 630 1GB GDDR3), running the BCI training task and the Vuzix iWear VR920 (Vuzix, NY, USA) head-mounted display (HMD) for displaying the feedback [Figure 6.1 a]. The HMD includes 640x480 twin LCD displays, 32-degree field of view (FOV), 3/4" eye relief and 5/16" eye box. The BCI set up was comprised of 8 active electrodes equipped with a low-noise bio-signals amplifier and a 16-bit A/D converter (256 Hz). The spatial distribution of the electrodes followed the 10-20 system configuration [on methods of clinical examination in electroencephalography, 1958] with the following electrodes over the sensory-motor areas [Figure 6.1 b]. The g.MOBIlab biosignal amplifier (g.tec medical engineering GmbH, Graz, Austria) was connected via Bluetooth to the desktop computer for the EEG signal acquisition and processing through OpenVibe platform [Renard et al., 2010]. For all sessions, a Common Spatial Patterns (CSP) filter was used for feature extraction. Linear Discriminant Analysis (LDA) was used for the classification of two classes (left — right-hand imagery). The classified data were transmitted to the RehabNet Control Panel (Reh@Panel) [Vourvopoulos et al., 2013] through the Virtual Reality Peripheral Network (VRPN) protocol [Taylor et al., 2001] to log the data and send the control signal to the online feedback module.

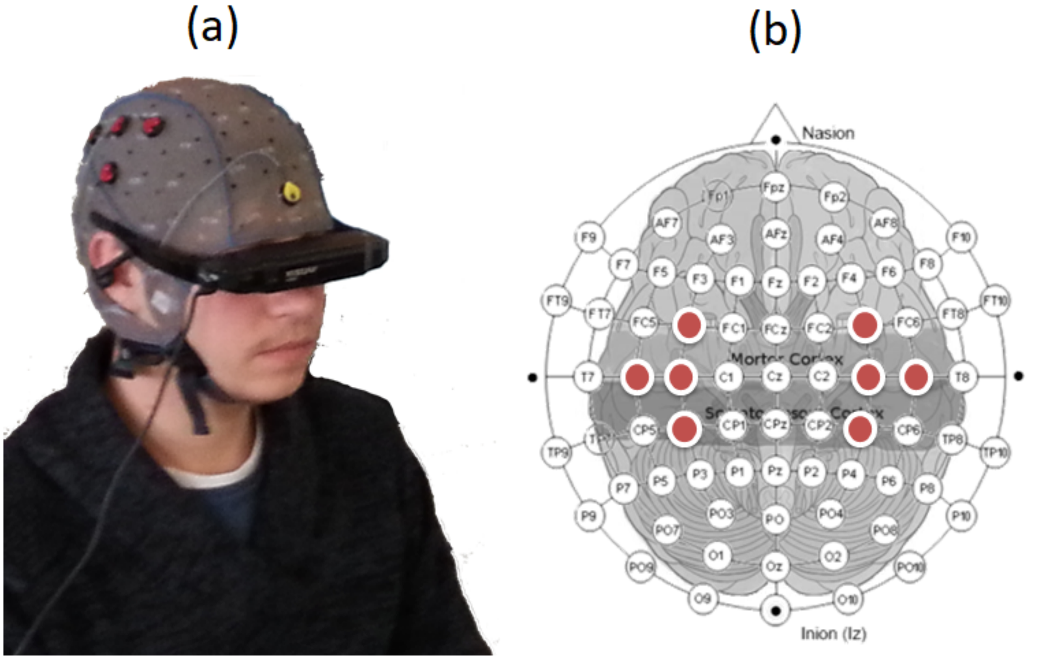

Figure 6.1: Headset setup and EEG electrode position. (a) User setup with EEG cap and HMD for displaying the feedback. (b) 10-20 configuration diagram of the electrodes over the motor and sensorimotor cortices: Frontal-Central (FC3, FC4), Central (C3, C4, C5, C6), and Central-Parietal (CP3, CP4)

The feedback was based on the Graz-BCI paradigm [Kalcher et al., 1996], which uses standard bars-and-arrows sequence [Figure 6.2(c)]. When an arrow appears on screen (left or right direction), the user has to perform mental imagery of the corresponding hand and this could involve mental grasping, throwing, waving, etc. The visualization should remain consistent during the whole duration of the training session in order to train a linear classifier that distinguishes left from right hand imagery. Each session included 5 main blocks (Figure 6.2): (1) 10-15 minutes of equipment setup and instructions; (2) subjects were exposed to an 8 minute MI-BCI training block followed by (3) a 5 minute rest; (4) a MI-BCI task of 8 minutes; and finally (5) subjects answered a set of self-report questionnaires. In total, each condition lasted approximately 50-60 minutes with 16 minutes of overall BCI exposure. During all blocks in all sessions, EEG data were logged synchronously and time-stamped including the different stimulation codes [Start of trial, End of trial, Left, Right, Feedback, Cross on screen] for offline analysis.

6.2.2 Questionnaires

Before the BCI training session, demographics and user data were gathered through three questionnaires:

1. The Edinburgh handedness inventory classifies users based on their handedness. It assesses left handed (-100% to -40%), ambidextrous (-40% to 40%) and right handed (40% to 100%), with a higher score corresponds to higher level of handedness either left or right [Oldfield, 1971].

2. The Vividness of Movement Imagery Questionnaire-2 (VMIQ2) [Roberts et al., 2008] was used in order to assess the feeling of the participant to perform an imagined movement (Kinesthetic Imagery). The Kinesthetic Imagery (KI) questions involve both upper and lower limb movements ranging from 1 ('no kinesthetic sensation'/'no image') to 5 ('as clear as executing an action'/'image as clear as seeing').

3. For assessing gaming experience we used the Gamer Dedication (GD) questionnaire, a 15 factor classification questionnaire as assessed though

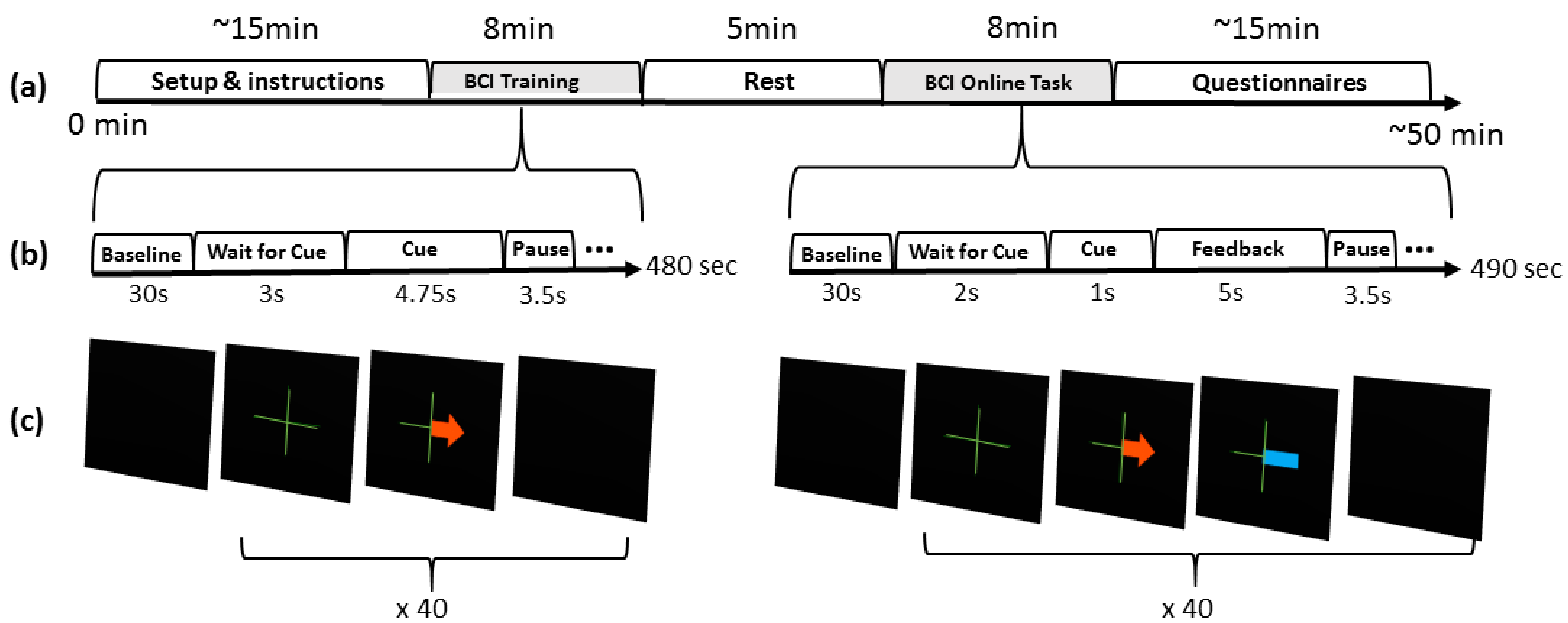

Figure 6.2: Experimental protocol overview. (a) Experiment protocol, starting with a 15 minute briefing and setup, followed by 8 minutes of BCI training, 5 minutes of rest, 8 minutes of online task, and questionnaires. (b) BCI calibration and motor-imagery task blocks. (c) Visual feedback stages with the Graz feedback for motor-imagery training.

a Likert scale between 1 to 5, in which participants were asked whether they "strongly disagree," or "strongly agree" with a series of statements [Adams and Ip, 2002].

6.2.3 Participants

The study consisted of a total of 20 participants with a mean age of 28 $\pm$ 2 years old, 16 male, 4 female. Participants were a voluntary sample, recruited based on their motivation to participate to the study, with no previous known neurological disorder. All subjects signed an informed consent to participate in the study and to publish their data. To group users based on their gaming experience, the GD questionnaire was used. Through this method the GD score was calculated based on the following formula:

$$GD = \frac{\sum_{j=1}^{n} w_j s_j}{\sum_{j=1}^{n} 5 w_j} \tag{6.1}$$

Where s = self-ranked score; and w = weight.

Since the GD score has not yet been validated for measuring gamer dedication, we gathered all 15 questions and we performed a Principal Component Analysis (PCA) to assess the consistency of the GD scores. PCA is a well-known technique for dimension-reduction and aims in reducing a larger set of variables into a smaller set of 'artificial' variables (called 'principal components') [Jolliffe, 2014]. The extracted components account for most of the variance in the original variables. From the PCA analysis, the principal component was highly significantly correlated with the GD final score (r = 0.98, p <0.001), meaning that the GD score is a sufficiently representative scale of gamer dedication for our sample. Following the scoring the Two-Step Cluster Analysis procedure was used to form gamer dedication groups based on the GD answers. Two-Step Cluster Analysis is an unsupervised machine learning task of inferring natural groupings or clusters within a dataset. From the clustering results we defined 2 balanced groups (10 users per group). These groups are further referred as 'Hardcore' and 'Moderate' gamers in the following sections.

6.3 Data Analysis

6.3.1 EEG Signal Processing

EEG signals were processed in Matlab (MathWorks Inc., Massachusetts, US) extracting the Power Spectral Density (PSD) following an Independent Component Analysis (ICA) for removing major artifacts related with power-line noise, eye blinking, ECG and EMG activities with the help of the EEGLAB toolbox [Delorme and Makeig, 2004]. The power spectrum was extracted every 500 ms using Welch's method with windows of 128 samples for the following frequency rhythms: Alpha (8 Hz - 12 Hz), Beta (12 Hz - 30 Hz), Theta (4 Hz - 7 Hz), and Gamma (25 Hz - 90 Hz). For the current analysis, and because we were only measuring from sensory-motor areas, data were averaged for all the channels for each experimental condition. Left and Right hemisphere electrodes were also aggregated to assess hemispheric asymmetries between groups (left hemisphere minus right hemisphere. From the extracted PSD the Engagement Index (EI) was computed for all participants during both training and online sessions. EI is a metric created at NASA Langley for evaluating operator engagement in automated tasks, and was validated by Prinzel et al. through a bio-cybernetic system for Adaptive Automation [Pope et al., 1995] and is widely used in EEG studies for assessing engagement [Berka et al., 2007]. The engagement index was computed from the EEG power spectrum according to equation 6.2.

$$EI = \frac{\beta}{(\alpha + \theta)} \tag{6.2}$$

$$Where\ \ \alpha = Alpha\ \ rhythm, \beta = Beta\ \ rhythm\ \ and\ \ \theta = Theta\ \ rhythm.$$

6.3.2 Statistical Methods

Normality of all data was assessed using the Shapiro-Wilk (S-W) normality test. For classifier performance, non-parametric statistical tests were used for the analysis because data deviated from normality. For the assessment of overall differences between three BCI sessions, a Friedman test was used on each dependent variable. For further pairwise comparisons, the Wilcoxon signed-rank test on each of our combinations was used. On EEG rhythm data, the S-W test revealed normality of the data ($p>0.05$). The data were analysed using a repeated measures ANOVA with a Greenhouse-Geisser correction due to Mauchly's Test of Sphericity violation. For all pairwise comparisons a Bonferroni correction was used to account for the number of comparisons. Effect sizes were computed on pairwise comparisons. For all statistical comparisons the significance level was set to 5% ($p<0.05$). Spearman correlations were performed between electrophysiological (EEG), demographics and questionnaire (GD, KI, and their sub-domains) data, with significance level set to 5% ($p<0.05$). All statistical analyses were done using IBM SPSS 20 (SPSS Inc., Chicago, IL, USA). Moreover, a Stepwise regression modeling approach was used to identify predictors that provide a good fit in the regression line based on their R-squared values and their statistical significance

($p<0.05$) between questionnaire, demographics and EEG data. The set of variables that were used for the multivariate linear regression includes (a) the subjective as reported through the questionnaires against (b) the EEG rhythms and the Engagement Index. The Stepwise coefficient estimation of the models was done using Matlab (MathWorks Inc., Massachusetts, US).

6.4 Results

To assess the strength and direction of association that exist between the EEG data (EEG rhythms, EI, hemispheric asymmetry), LDA classification score and the population data (Demographics, KI and GD answers), the Spearman rank-order correlation coefficient were calculated. Subsequently, a multilinear regression modeling analysis was used to identify predictors that can describe the relationship between dependent and independent variables.

6.4.1 What is the Relationship of User Profile and EEG Activity?

A. EEG Activity in Training Session

Demographic Data: EEG rhythms generated during training, Alpha, Beta, Theta, Gamma positively correlated with gender as age group correlated only with Gamma and handedness only with Theta rhythms (Table 6.1).

Kinesthetic Imagery Data: From the reported KI ability, a significant correlation between the classification performances was found during training with the reported KI ability for "swinging on a rope". In addition, a reverse correlation between the Engagement Index during training and the KI of the participant of "bending to pick up a coin". Finally, users with increased KI of "walking" formed a reverse correlation the Engagement Index and with the hemispheric asymmetry of Theta rhythm during training (Table 6.1).

Gamer Dedication: From the GD answers, the "preference towards violent/action games" correlates significantly with Alpha, Beta, Theta during training. "Discussing games with friends/bulletin boards" and users that have "comparative knowledge of the industry" have a significant correlation with high Engagement Index. On KI, significant reverse correlations are formed only for scores from users that are "technologically savvy" and "willing to pay" for games. Furthermore, users that "play games over many long sessions" have increased hemispheric asymmetry in Gamma. Those who have the "desire to modify or extend games in a creative way" have increased hemispheric asymmetry in all rhythms, namely for Alpha, Beta, Theta, Gamma. Scores from users that "play for the exhilaration of defeating (or completing) the game" have increased hemispheric asymmetry in Alpha, Beta, Theta. Similarly, score from users which are "engaged in competition with themselves, the game, and other players" have stronger and increased hemispheric asymmetry in Alpha, Beta, Theta (Table 6.1). Finally, classification score from the training session is significantly reversed correlated with the hemispheric asymmetry of Alpha, Beta, and Theta.

Table 6.1: Significant correlations between demographic data and subjective answers (rows) with extracted EEG related data (columns) and kinesthetic imagery for both training and online session.

	Alpha Training	Beta Training	Theta Training	Gamma Training	Alpha Online	Beta Online	Theta Online	Gamma Online	EI Training
GD: I prefer violent/action games	.599**	.496*	.664**		.571*	.477*	.680**		
GD: I discuss games with friends/ bulletin boards							.472*		.566*
GD: I have comparative knowledge of the industry									.635**
KI: Walking					-.647**		-.517*		-.486*
KI: Bending to pick up a coin									-.520*
Gender	.495*	.566*	.566*	.471*	.542*	.613**	.519*	.566*	
Age Group				.523*					
Education					.550*	.520*			
Handedness		.539*		.587**	.702**	.662**	.662**		
Sport Gym									

Table 6.1 continued

	EI Online	KI	Theta Hemi. Asymm. Training	Gamma Hemi. Asymm. Training	Alpha Hemi. Asymm. Online	Beta Hemi. Asymm. Online	Theta Hemi. Asymm. Online	Gamma Hemi. Asymm. Online	LDA Training
GD: I discuss games with friends/bulletin boards	.484*								
GD: I have comparative knowledge of the industry	.553*								
GD: I have the latest high-end computers/consoles	.635**					.498*		.649**	
GD: I am technologically savvy		-.489*							
GD: I am willing to pay		-.501*							
GD: I play games over many long sessions				.489*				.467*	
GD: I have the desire to modify or extend games in a creative way					.669**	.733**	.722**	.567*	
GD: i play for the exhilaration of defeating (or completing) the game					.459*	.512*	.472*		
GD: I am engaged in competition with myself, the game, and other players					.612**	.580**	.567*		
KI: Swinging on a rope									.484*
KI: Walking			-.456*						
Handedness						.461*		.527*	
Sport Gym					-.478*	-.498*	-.498*		

B. EEG Activity in Online BCI Session

Demographic Data: EEG rhythms produced during the online session: Alpha, Beta, Theta, Gamma form a significant relationship with gender and education with Alpha and Beta rhythms. Furthermore, participants involved in a sport or frequent gym visits, have a significant reverse correlation with the hemispheric asymmetry that occurred during the online session. Namely, in the Alpha, Beta and Theta rhythms. For handedness, a strong positive significant correlation is found for all EEG rhythms during the online session (Alpha, Beta, Theta, Gamma), and also with the hemispheric asymmetry in Beta and Gamma. Overall, gender, education and handedness affect EEG rhythm modulation with sports and handedness to strongly affect also the hemispheric asymmetry in EEG rhythm activation (Table 6.1).

Kinesthetic Imagery Data: The KI of the participant with increased KI of "walking" formed a reverse correlation with the produced Alpha and Theta rhythms, similar to the training session (Table 6.1).

Gamer Dedication: Similar as in training session, the "preference towards violent/action games" correlates significantly with all EEG rhythms except Gamma during the online session. Also, "Discussing games with friends/bulletin boards" correlates significantly with the Engagement and additionally with increased Theta rhythms. Score from users that have "comparative knowledge of the industry" have a strong correlation with high Engagement Index. Users which have the "latest high-end computers/consoles" form a strong correlation with the online Engagement Index and with hemispheric asymmetry for Beta and Gamma. On KI, significant reverse correlations are formed only for scores from users that are "technologically savvy" and "willing to pay". Furthermore, users that "play games over many long sessions" have increased hemispheric asymmetry in Gamma rhythms similarly as in the training session. Also, those who have the "desire to modify or extend games in a creative way" have increased hemispheric asymmetry in all rhythms. Scores from users that "play for the exhilaration of defeating (or completing) the game" have also increased hemispheric asymmetry in Alpha, Beta, Theta and finally, score from users which are "engaged in competition with themselves, the game, and other players" have stronger and increased hemispheric asymmetry in Alpha, Beta, Theta (Table 6.1).

6.4.2 Can EEG Activity be predicted from User Profile?

A stepwise regression modeling was used to identify predictors of GD and KI from EEG activity through the different rhythms, engagement index and hemispheric asymmetry and also the overall performance (see Table 6.2). The most significant predictor for the online performance (R^2 =.243) is the score related to the level of tolerance or frustration as reported through the GD questionnaire. The Alpha rhythm modulation during training (R^2 =.327) is related with the users which prefer violent/action games as-well-as the Alpha during the online session (R^2 =.524), combined with the user score related with the exhilaration of defeating (or completing) the game. Beta rhythm (R^2 =.564) during the online session is related with the preference to violent/action games, comparative knowledge of the industry, and engagement in competition with themselves the game, and other players. Finally, Theta activity in the online session (R^2 =.418) is related with score of users that prefer violent/action games. For KI (R^2 =.261), the score of users that are technologically savvy is a significant predictor. Engagement index during training (R^2 =.609) is related with users that have comparative knowledge of the industry and with users that have a hunger for gaming-related information. Engagement index during the online session (R^2 = .612) is related with the score of users that have the latest high-end computers/consoles and the score of them that have a hunger for gaming-related information. Concerning hemispheric asymmetry, from training data, the hemispheric difference of Theta (R^2 =.230) is related with the score of users that are technologically savvy and for Gamma (R^2 =.242) is related with the score of them which play games over many long sessions. From the hemispheric asymmetry as recorded during the online session, asymmetry of Alpha (R^2 =.583) is related with the score for those which play games over many long sessions and have the desire to modify or extend games in a creative way. For Beta (R^2 =.579), users which play games over many long sessions and have the desire to modify or extend games in a creative way have a significant relationship. For Theta (R^2 =.455), users which have the desire to modify or extend games in a creative way is significantly related, and for Gamma (R^2 =.419), the score of users which have the latest high-end computers/consoles is related with the hemispheric asymmetry. Finally, training classification performance (R^2 =.292) can be better predicted by the hemispheric asymmetry of Theta.

Table 6.2: Stepwise Linear Regression coefficients between Gamer Dedication answers (columns) and extracted EEG data and kinesthetic imagery (rows)

Dependent Variable (R Square) / Independent Variables (Coeff.)	GD: I am much more tolerant of frustration	GD: I am technologically savvy	GD: I prefer violent/action games	GD: I play for the exhilaration of defeating	GD: I have comparative knowledge of the industry	GD: I am engaged in competition with	GD: I have the latest -end	GD: I have a hunger for gaming-related	GD: I am willing to pay	GD: I play games over many long sessions	GD: I have the desire to modify or extend games in a creative way
LDA Online (.243)	-1.759										
KI (.261)		-4.753									
Alpha Training (.327)			2.029								
Alpha Online (.524)			3.093	1.266							
Beta Online (.564)			3.305		-1.748	1.227					
Theta Online (.418)			2.518								
EI Online (.609)							0.012	-0.009			
EI Training (.612)					0.009				-0.007		
Theta Hemi. Asymm. Training (.230)		1.099									
Gamma Hemi. Asymm. Training (.242)										1.268	
Alpha Hemi. Asymm. Online (.583)										1.2	2.344
Beta Hemi. Asymm. Online (.579)										1.244	2.231
Theta Hemi. Asymm. Online (.455)											2.651
Gamma Hemi. Asymm. Online (.419)							2.068				

6.5 Discussion

From current results we have identified important user-traits that can be used in the design of MI-BCI training within a gamified task. So far, our findings show: (1) contrasts of different user-groups over time and (2) relationship between electrophysiological data with gaming experience, KI ability and demographic data.

From the demographic data, gender related correlations can be identified, strongly associated with all EEG rhythms in both training and online task. Handedness was related mostly with EEG activity modulation and asymmetry through the online session. Based on previous research, asymmetry in the Alpha rhythm is task-dependent and extends to a broader range of tasks [Galin et al., 1982], also to be depended upon gender and familial handedness [Glass et al., 1984]. It was also identified that users which exercise frequently have reduced hemispheric asymmetry, which is consistent with previous findings that show differences in all EEG rhythms in users with increased physical activity [Lardon and Polich, 1996]. Finally, the level of education correlated significantly with the amplitude of online Alpha and Beta rhythms, important for motor-imagery training, which are modulated during sensorimotor activation.

For KI, the training performance is correlated with the swinging on a rope KI-score, and engagement index is correlated during training with bending to pick a coin score. The most important KI relationship was between users with increased walking KI score and a reverse correlation with online Alpha and Theta, engagement index during training and hemispheric asymmetry on Theta rhythms. Interestingly, similar correlations occurred for users performing sports, suggesting a relationship between physical activity and KI ability of lower limbs.

For GD multiple correlations related to hemispheric asymmetry were identified, for users that play games for long sessions, modify games creatively, are very competi-tive and truly engaged to the competition in general. Previous studies have shown that hemispheric asymmetries enhance the performance of fine motor tasks and triggers changes in motor learning [Garry et al., 2004]. Therefore, users engaged in a competitive manner and in long sessions of game-play could present enhanced motor-related EEG modulation, leading to increased motor-learning. Finally, users which prefer violent and/or actions games have an increased ability to modulate all EEG rhythms in both training and online sessions. Through linear regression modeling, we identified that competitiveness and preference to violent/action games are significant predictors for the EEG rhythm modulation that is mostly activated during MI (i.e. Alpha and Beta rhythms). Furthermore, increased addiction (play games over long hours) is a predictor for increased hemispheric asymmetry that could lead in increased BCI performance.

6.6 Conclusions

Experimental results of this study indicate that demographic traits like gender, handedness, experience of action and violent games affect the activity patterns of sensorimotor-related EEG rhythms during a MI task. Concerning BCI performance, results showed that increased performance is related with higher tolerance to frustra-tion, and also to users with increased KI of rope swing and bike riding. Moreover, long gaming sessions and addiction seem to increase hemispheric asymmetries -related from previous research to increased performance of fine motor tasks- and it was showed that increased hemispheric asymmetry can be a more valuable predictor of BCI performance than specific EEG rhythm modulation. Increased gaming experience might not directly increase the performance in an MI-BCI paradigm, but it can provide faster learning. Summarizing, with current results we can link the impact of demographics in EEG modulation during a motor-imagery session, identifying a clear influence of the user profile in EEG rhythms activity patterns. Moreover, a relationship between video-game practice and BCI performance was identified. This will help us not only to identify possible causes of BCI illiteracy but also to provide inclusion criteria for BCI training and adaptation of current BCI training protocols. Consequently, current results provide a first step into user-centered neurogame design using EEG-based motor-imagery as a primary input but also to open a way into exploring the effect in augmented/virtual reality applications and its effect on embodied cognition. This underexplored possibility for BCI training has a great potential not only for games in the entertainment domain but also for utilizing these techniques in the health domain for users with neurological disorders through with the use of virtual tools and serious games. Recent development in mixed reality technology Overall, since we know which traits of player profile can influence EEG rhythms activity patterns during a motor-imagery task and we have modeled the relationship between video-game practice and player profile with BCI performance, we can embed current findings in neurogame design for enhanced performance.

Chapter 7

Comparing MI Enhancement Techniques: The Effect of Virtual Reality and Motor Priming in BCI Training

7.1 Introduction

Despite the increased attention that BCI technology has had with the launch of low-cost commercial EEG devices in the last few years, BCI technology is hardly used outside laboratory environments [Lotte et al., 2013b]. Unfortunately, BCIs are not yet as accurate as other types of interfaces [Lotte, 2012], and users require a training period up to several months to achieve accuracies of 65%–80% using cortical potentials [Wolpaw et al., 2002]. Although accuracy varies among the different BCI paradigms, most are not 100% accurate, they require extensive training, and have low information transfer rates and long response delays [Friedman, 2015]. For instance, MI-BCI requires long training trials and settings are subject specific. As consequence, long and repetitive training sessions can result in user fatigue and declining performance over time. In addition, prolonged training is problematic in generating the EEG oscillatory rhythms modulated during MI, such as Mu and Beta rhythms [Schomer and Silva, 2011]. New findings in MI experimentation have shown that increased vividness of imagery is strongly associated with the neural activity in motor-related areas [Wriessnegger et al., 2014] and that the kinesthetic imagination of movement is preferable over just visual imagination, resulting in increased MI-BCI performance [Neuper et al., 2005]. Unfortunately, there is a limited understanding of how these factors affect the activity patterns of motor-related areas. Recent studies have shown that physical activity prior to an MI task (motor priming) facilitates the engagement of motor networks on the subsequent MI task [Meyer and Schvaneveldt, 1971]. It has been shown that during feedback presentation EEG synchronization patterns increase hemispheric asymmetry compared to control sessions without feedback [Neuper et al., 1999]. In addition, hemispheric asymmetry is related to the increased performance of fine motor tasks and specifically left hemisphere changes are related to motor learning [Garry et al., 2004]. However, different studies had different experimental setups and it is not clear how we can improve the design of an MI-BCI paradigm. Moreover, there is a lack of systematic studies dedicated to the actual aspects of the experimental (training) task, focusing mostly on the technical aspects of the system. Therefore, in the area of neurorehabilitation, there is an urgent need to identify the key elements for a successful MI-BCI training using specific criteria for motor rehabilitation for including patients with severe hemiparesis. This leads to questions such as, (1) How can we include patients with low level of motor control, (2) how can we maximize both performance and sensorimotor activation, and (3) how can we promote adherence to MI-BCI training? In order to overcome some of the limitations of current BCI systems, we performed a study based on a novel prototype that makes use of multimodal feedback, in an immersive VR environment delivered through a state-of-the-art Head Mounted Display (HMD), integrated in a MI-BCI motor training task (left — right hand imagery) [Vourvopoulos et al., 2015a]. To achieve maximum engagement of sensory-motor networks in an MI-BCI motor rehabilitation task, we assessed the role of motor priming and multimodal VR feedback compared to a control condition. In this study, we included naïve subjects, with no previous exposure in BCI, in order to have a first-time user experience (FTUE). Based on the analysis of the literature we expect that:

1. Through an immersive multimodal VR environment and motor priming, we can maximize the engagement of sensory-motor networks important in neurorehabilitation, due to the enhanced modulation of the same cortical areas that are activated during actual motor preparation and execution.

2. We can quantify the relationship between users' electrophysiological data and psychophysiological responses, important for identifying which patient profile can benefit the most from an immersive BCI-VR setup for MI training.

7.2 Methods

7.2.1 Experimental Design

In this experiment we used a within-subject design. The protocol consisted of 3 BCI conditions to which users were exposed in a randomized order, and their EEG activation patterns were then also compared to the activity during overt motor-execution. Each participant performed one condition per day, completing all conditions in 3 days. Each condition included 5 main blocks (Figure 7.1): (1) 10-15 minutes of equipment setup and instructions; (2) subjects were then exposed to an 8 minute MI-BCI calibration block followed by (3) a 15 minute pause; (4) a MI-BCI task of 8 minutes; and (5) subjects answered a set of self-report questionnaires. In total, each condition lasted approximately 60-70 minutes with 16 minutes of BCI exposure. During all blocks in all conditions, EEG data were logged synchronously and time-stamped including the different stimulation codes [Start of trial, End of trial, Left, Right, Feedback, Cross on screen] for offline analysis.

7.2.2 Experimental Conditions

In our design of the BCI setup, we incorporated properties that are recommended as a good instructional design in BCI training [Lotte et al., 2013b]. In all conditions we presented the user only with the correct classified action for enhancing the feeling of competence, we provided a clear and meaningful task through the virtual task paradigm, the task was self-explanatory, simplified and intuitive, with progress of achievement, challenging but achievable, and finally in an engaging 3D virtual environment. All 3 BCI conditions were designed based on the Graz-training paradigm [Kalcher et al., 1996]. The control condition incorporated the Graz-training with abstract bars-and-arrows

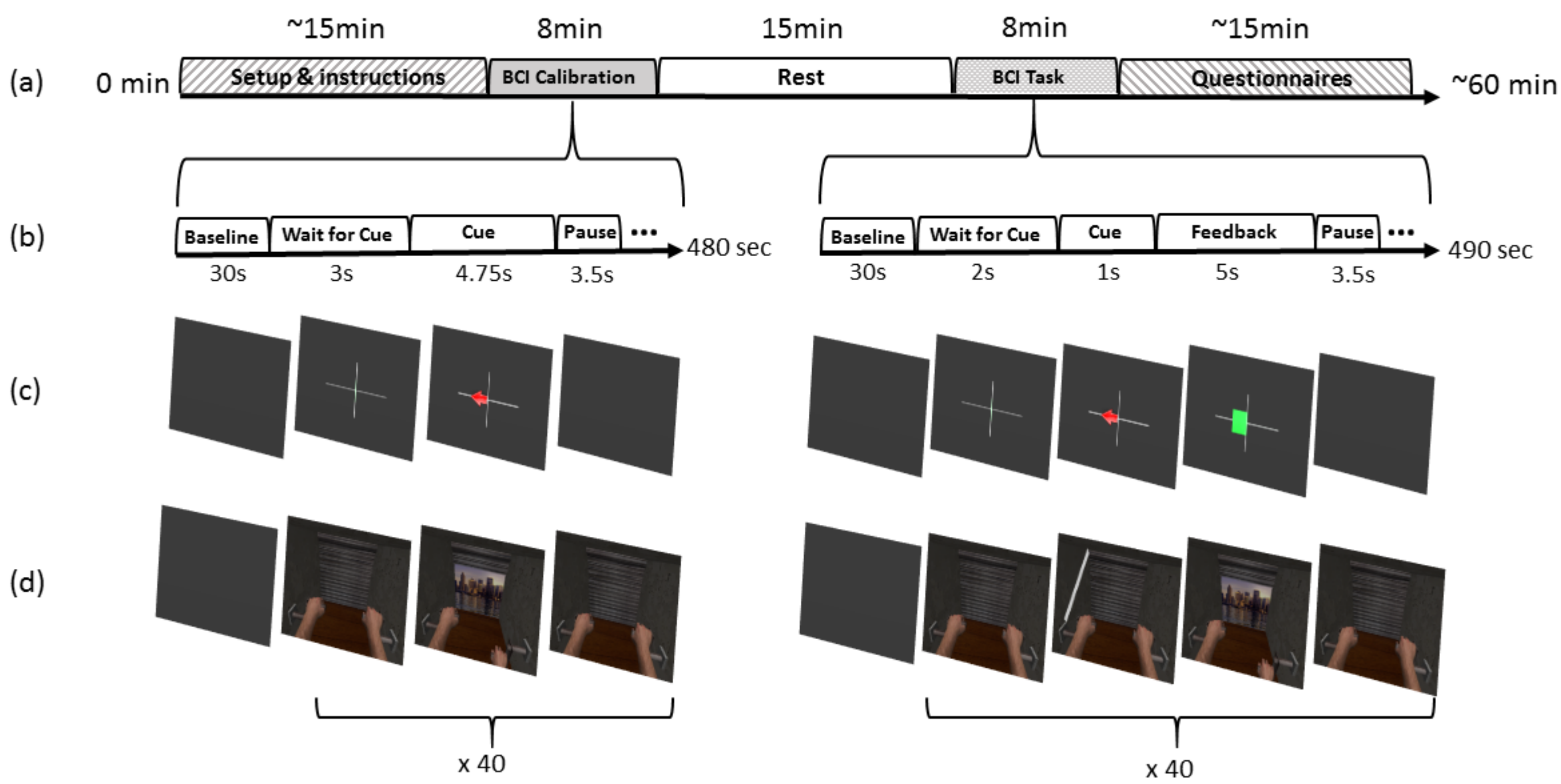

Figure 7.1: Experimental Setup overview. (a) Experiment timeline, starting with a 15 minute briefing and setup, followed by 8 minutes of BCI calibration, 15 minutes of rest, 8 minutes of online task performance, and questionnaires. (b) BCI calibration and MI task blocks. Starting with baseline measurement, the user waits for a cue followed by a pause (repeated 40 times, 20 per class). (c) Stages for the Control condition with the standard arrows-and-bars feedback. (d) Stages for the VR training feedback, replacing the directional arrows with virtual hands performing a task in a 3D immersive environment.

feedback, and for the VR version we used ambient and event sounds and a virtual representation of two hands performing the motor action. Three experimental conditions were designed with different feedback and priming mechanisms: multimodal VR with motor priming, multimodal VR, and standard MI [1]. For all conditions, a total of 10 repetitions (of approximately 4 seconds duration, followed by a 2 second pause) of motor-execution/mental simulation for each hand were performed and presented always through a HMD.

1. Multimodal Virtual Reality with Motor Priming (VRMP)

In this condition, users were asked to carry out a motor-execution task for 8 minutes using an immersive virtual reality environment before performing the MI-BCI calibration block. For this, we combined the HMD with a natural user interface that tracked hand and finger movements to enable a natural interaction of the participants with the virtual environment, by mapping the movement of their own hands to VR with an update frequency of the visual feedback at 30Hz Figure 7.2(a). The motor-execution task, a virtual garage, involved the rotation of a virtual lever through circular movements for opening a large garage door. The virtual environment included spatial sounds related with the movement of the door and the lever. The sounds generated by the chain mechanism and other mechanical sounds, were activated through the rotation of a handle that controls the opening of a virtual garage door. Before each repetition, the user was informed of which hand should be used to open the garage door. This stage will be further referred as motor priming (MP) block. Subsequently, a MI-BCI calibration block took place to determine the best MI classifier parameters based on the same VR task

[1] `https://www.youtube.com/watch?v=3tBIDN4uskQ`

and feedback as used during MP. In this block, the user had to imagine the same movement performed previously in the MP block. Finally, the same virtual environment was used for a MI-BCI online block, in which the user could directly control the virtual arms through the BCI interface using MI.

2. Multimodal Virtual Reality (VR)

In this condition, users were asked to only carry out the MI-BCI calibration block and the online MI-BCI task block as in the previous condition, but without the prior MP (Figure 7.2 (b)).

3. Control - Standard Motor Imagery

In this condition, a standard MI-BCI paradigm was used, providing a control condition for the other conditions to be compared with. Hence, this condition followed the same protocol as the VR condition, but instead of the VR component only simple bar-and arrow-elements without sounds (the so-called Graz visualization) were used as feedback mechanisms (Figure 7.2(c)). Yet, the MI task consisted in the motor imagery of the same upper-limb movements as described in conditions VRMP and VR and was presented through the same HMD.

7.2.3 Experimental Setup

The experimental setup was composed by a desktop computer (OS: Windows 8.1, CPU: Intel® Core™ i5-4440 at 3.3 GHz, RAM: 8GB DDR3 1600MHZ, Graphics: Nvidia GT 630 1GB GDDR3), running the 3 different MI-BCI training conditions described above. All visual and auditory feedback was developed with the Unity 3D game engine (Unity Technologies, San Francisco, USA). For hand and finger tracking during the MP block, the Leap Mo-

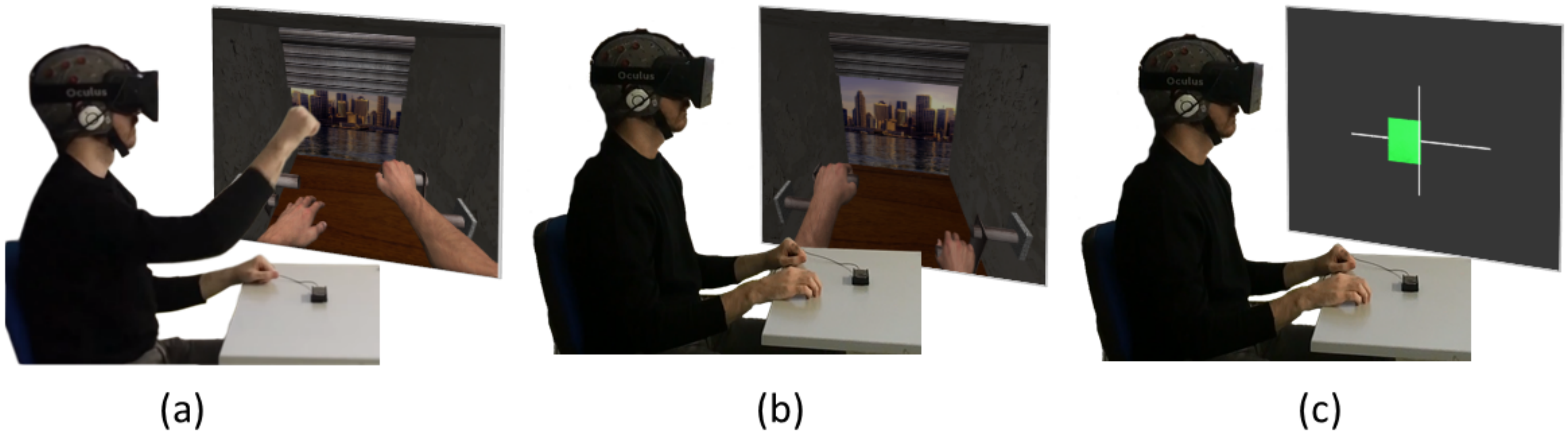

Figure 7.2: MI-BCI training conditions. (a) VRMP: the user has to perform motor priming by mapping his/her hand movements into the virtual environment. (b) VR: the user has to perform training through simultaneous motor action observation and MI, before moving to the MI task were he/she has to control the virtual hands through MI. (c) Control: MI training with standard feedback through arrows-and-bars.

tion controller (Leap Motion, Inc., San Francisco, California, United States) was used to map hand and finger movements to the virtual counterparts. A stereo headset for spatial sound was used in VR and VRMP conditions. The Oculus Rift DK1 HMD (Oculus VR, Irvine, California, United States) was used for all conditions, regardless of the feedback modality. The BCI set up consisted of 8 active electrodes equipped with a low-noise biosignal amplifier and a 16-bit A/D converter at 256 Hz (g.MOBIlab biosignal amplifier, gtec, Graz, Austria). The spatial distribution of the electrodes followed the 10-20 system configuration with the following electrodes over the sensory-motor areas: FC3, FC4, C3, C4, C5, C6, CP3, and CP4. The signal amplifier was connected via bluetooth to a laptop computer (CPU: Intel® Core™ i3-3217U at 1.80 GHz, RAM: 8GB DDR3 1600MHZ, Graphics: Intel® HD Graphics 4000) for the EEG signal acquisition and processing through the OpenVibe platform [Renard et al., 2010]. For all conditions, a Common Spatial Patterns (CSP) filter was used for feature extraction, based on the mutual diagonalization of each covariance matrix for each class to be discriminated [Koles, 1991]. CSP has been shown to deliver better performance in MI experiments [Pfurtscheller et al., 1999]. In addition, Linear Discriminant Analysis (LDA) was used for the classification of the two classes (left — right hand imagery) from the feature vector. LDA reduces the dimensionality of the data and establishes a surface decision in the feature space which separates data into two groups, each one related to one class [Fukunaga, 1990]. Finally, the classified data were transmitted to the RehabNet Control Panel (Reh@panel) [Vourvopoulos et al., 2013] through the VRPN protocol [58] to control the virtual environment. The RehabNet Control Panel is a free tool that acts as a device router to bridge a multiple interfaces with virtual environments.

7.2.4 Participants

A total of 9 right handed healthy participants (8 male, 1 female) with a mean age of 27 $\pm$ 2 years old participated in the study. Participants were recruited based on their motivation to participate, with no previous known neurological disorder. We included only naïve subjects, with no previous exposure in BCI, to have a first-time user experience (FTUE). This was done in order to minimize any bias by previous experienced in MI in neurofeedback and because our target population has no prior BCI exposure. All participants were students and staff from the University of Madeira and were recruited at the Madeira Interactive Technologies Institute. The experiments were approved by the Ethics Committee of the Public Health System of the Autonomous Region of Madeira, Portugal (SESARAM), with decision number: 15/2015. All subjects were informed and signed an informed consent to participate and to publish their data according to the Declaration of Helsinki.

7.2.5 Questionnaires

Subjective experience data was gathered through three questionnaires: the Presence Questionnaire, the Vividness of Movement Imagery Questionnaire-2, and the NASA TLX.

- The Presence Questionnaire (PQ) is a tool that measures the degree to which individuals experience presence in a virtual environment and the influence of possible contributing factors to the intensity of the experience [Witmer and Singer, 1998]. PQ has 24 questions in a seven-point Likert scale to assess items such as realism, possibility to act and sounds. Items related to haptic assessment were excluded because this aspect was not addressed in our experiment.

- Vividness of Movement Imagery Questionnaire-2 (VMIQ2) [Roberts et al., 2008] was used to assess the Kinesthetic Imagery ability of the participant. VMIQ comprises 12 questions to rate vividness of different items in a 5-point scale. Participants had to report how clear was the image obtained by imagining themselves do the following movements (Kinaesthetic imagery): walking, running, kicking a stone, bending to pick up a coin, running up-stairs, jumping sideways, throwing a stone into water, kicking a ball in the air, running downhill, riding a bike, swinging on a rope, and jumping off a high wall. The VMIQ has been previously used to determine differences in neural activation patterns between vivid and non-vivid imagery [Marks and Isaac, 1995].

- Finally, the NASA TLX questionnaire was used to measure task load through a number of subscales [Hart and Staveland, 1988]. These subscales include Mental Demands, Physical Demands, Temporal Demands, Performance, Effort and Frustration.

7.2.6 Data analysis

1. Power Spectral Density (PSD) Estimation

In order to remove major artifacts related with eye blinking and muscular activity, a manual cleaning of the signal in the time domain was performed, followed by a component rejection process. The component rejection was performed by using Independent Component Analysis (ICA) with the help of the EEGLAB toolbox [Delorme and Makeig, 2004]. With the use of ICA we rejected components responsible for major artifacts of either endogenous (muscle, jaw clenching, eye movement) or exogenous source (AC power line). EEG rhythms were processed by extracting the Power Spectral Density (PSD) of the signals in Matlab (MathWorks Inc., Massachusetts, US). The power was extracted every 500 ms using Welch's method with windows of 128 samples for the following frequency bands: Alpha (8 Hz - 12 Hz), Beta (12 Hz - 30 Hz), Theta (4 Hz - 7 Hz), Low Gamma (25 Hz - 45 Hz), and High Gamma (55 Hz - 90 Hz). For the current analysis and because we were only measuring from sensory-motor areas, data were averaged for all the channels for each experimental condition. Moreover, left and right hemisphere electrodes were aggregated to assess hemispheric differences between conditions.

2. Statistical analysis

The following metrics are used as dependent variables in our experimental design: EEG rhythm amplitude, MI classifier performance, Workload, and Kinesthetic Imagery.

- EEG Rhythms: We used the mean PSD from each EEG frequency band for each condition.
- MI classifier performance: From the LDA classification accuracy on both the calibration and the online task blocks, we calculated the mean classification accuracy per condition as a percentage.
- Workload: We used the sum of all sub-elements of the TLX questionnaire to extract the Workload for each participant on each condition.
- Kinesthetic Imagery: We used the sum of all sub-elements per user to extract the overall Kinesthetic Imagery.

Normality of the distribution of all data was assessed using the Shapiro-Wilk (S-W) normality test, recommended for tests with a sample size of less than 50 [Elliott and Woodward, 2006]. For classifier performance, and because the data deviated from normality, non-parametric statistical tests were used for the analysis. For the assessment of overall differences between the three experimental conditions, a Friedman test was used on each dependent variable. For further pairwise comparisons, the Wilcoxon signed-rank test on each of our combinations was used. On EEG rhythm data, the S-W test revealed normality of the data ($p>0.05$). We therefore analyzed the data using a repeated measures ANOVA with a Greenhouse-Geisser correction due to Mauchly's Test of Sphericity violation. For all pairwise comparisons a Bonferroni correction was used to account for the number of comparisons. Effect sizes were computed on pairwise comparisons. For all statistical comparisons the significance level was set to 5% ($p<0.05$). All statistical analysis was done using IBM SPSS 20 (SPSS Inc., Chicago, IL, USA). Spearman correlations were performed between the mean PSD from all EEG rhythms (Alpha, Beta, Theta, Gamma) and questionnaire (Workload, Kinesthetic Imagery, and their sub-domains) data, with a significance level set to 5% ($p<0.05$).

3. Multivariate linear regression

A Stepwise regression modelling approach was used to identify electrophysiological predictors that provide a good fit based on their statistical significance ($p<0.05$) between subjective (questionnaires) and objective (EEG) data. The set of variables that were used for the multivariate linear regression includes (a) the subjective experience as reported through the questionnaires against (b) the EEG rhythms. The Stepwise coefficient estimation of the models was done using Matlab (MathWorks Inc., Massachusetts, US).

7.3 Results

In the following section, results concerning EEG activity, classification performance and questionnaire answers are illustrated for all conditions. In addition, electrophysiological correlates between subjective and objective data are assessed in order to understand how we can maximally engage motor areas in an MI-BCI task.

7.3.1 Effect and Impact of Different MI-BCI Experimental Paradigms

To assess the difference between all conditions, we compared the different EEG rhythms, the classification score (the ability of the classifier to identify correctly one of the two classes of our motor-imagery task), and the hemispheric asymmetry for (1) motor-execution during MP, (2) VRMP condition, (3) VR condition, and (4) Control condition. In this analysis, (1) and (4) are used both as controls for comparison to standard MI-BCI feedback and to assess resemblance with actual motor-execution. The latter is particularly interesting since we aim for a MI-BCI paradigm that is able to retrain the same motor networks that are responsible for actual movement.

7.3.2 Calibration Block

EEG rhythms: A repeated measures ANOVA determined that mean EEG rhythms differed significantly across conditions for: Alpha ($F(2.524, 20.191) = 4.800$, $p < 0.05$), Beta ($F(1.599, 12.796) = 7.541$, $p < 0.05$), Theta ($F(1.874, 14.990) = 7.615$, $p < 0.05$), low Gamma ($F(1.713, 13.701) = 11.639$, $p < 0.05$), and high Gamma ($F(1.617, 12.938) = 6.869$, $p < 0.05$) [Figure 7.3(a)]. EEG rhythms during calibration show a convergence of brain activation for VR and

VRMP conditions towards overt motor-execution. Overall, EEG data show a clear trend with overt motor-execution and Control condition at opposite ends and VR and VRMP in between, being the latter the closest to motor-execution. Post hoc tests revealed that the mean EEG rhythm on the Alpha band differed significantly between VRMP and Control conditions. For the Beta band, a significant difference was found between both motor-execution and VRMP conditions with Control. For the Theta band, motor-execution was significantly different from both VR and Control conditions, and VRMP from Control. In Lower Gamma, motor-execution was significant different from VRMP and VR, as VRMP was significantly different from Control. Interestingly, in Lower Gamma, the above trend was altered, with the mean power of overt motor-execution displaying the lowest values. Finally, for Higher Gamma, there was a significant difference for both motor-execution and VRMP conditions with Control.

Classification Score: The MI-BCI calibration data revealed that the multimodal setup with motor priming condition (VRMP) provided the highest performance (Mdn = 65.8, IQR = 3.32) when compared with the VR only condition (Mdn = 64.5, IQR = 5.41) and control condition with the traditional feedback (Mdn = 62.3, IQR = 7.63) Figure 7.4. However, these differences are small and a Friedman test revealed no statistical difference

Hemispheric Asymmetry In the Calibration block, we observe the same convergence pattern towards motor-execution present in the previous EEG analysis for all frequency bands [Figure 7.5 (a)]. A repeated measures ANOVA determined that mean difference of hemispheric asymmetry, was not statistically significantly different between conditions for calibration, in Alpha ($F(2.219, 17.754) = 0.865$, $p = 0.448$), Beta ($F(1.905, 15.242) = 0.998$, $p =$

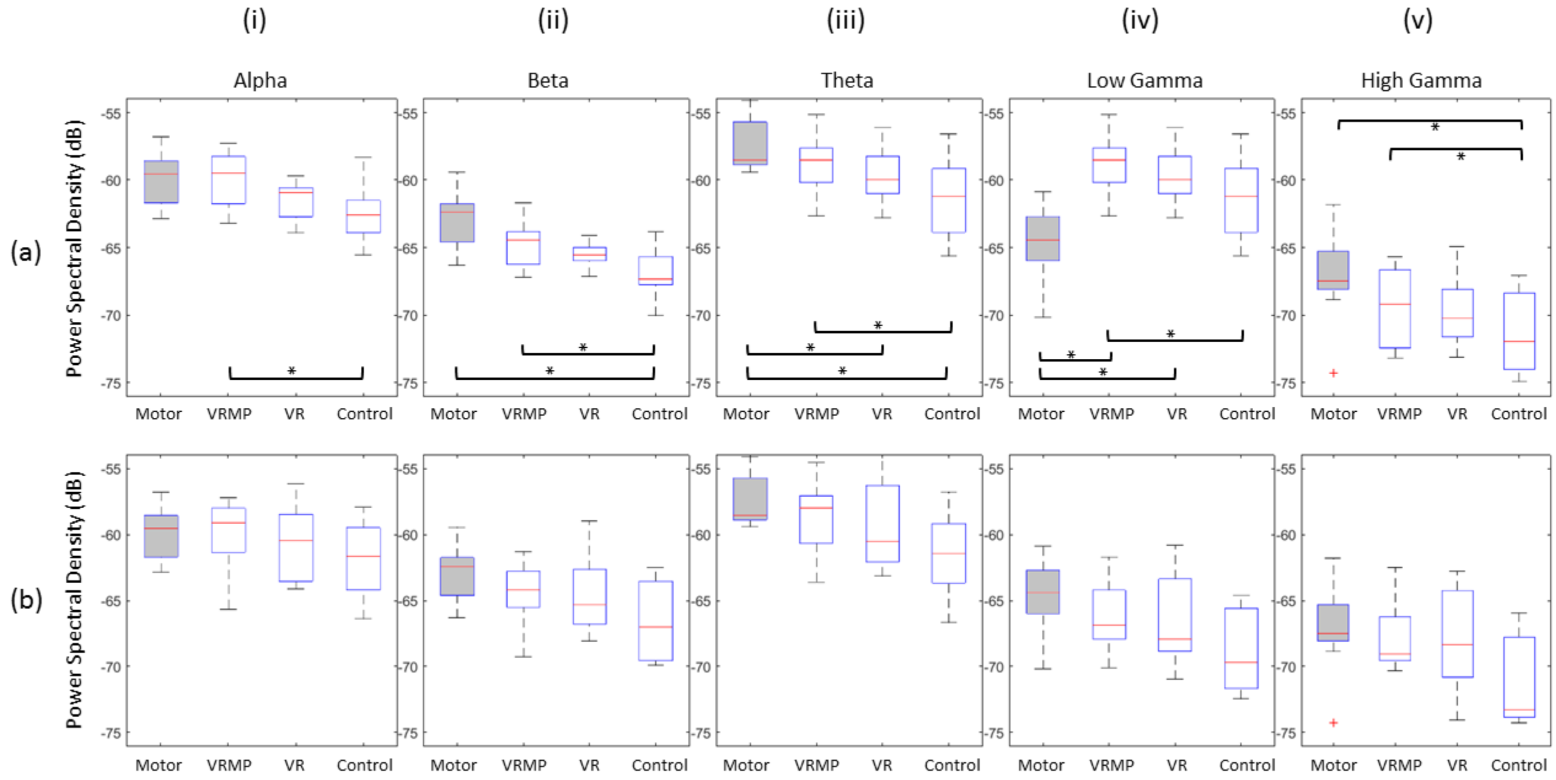

Figure 7.3: Power Spectral Density (PSD) of all EEG bands. (a) EEG band modulation during the calibration session. (b) EEG band modulation during the MI task.

0.388), Theta ($F(1.941, 15.528) = 0.960$, $p = 0.402$), low Gamma ($F(2.083, 16.667) = 0.719$, $p = 0.507$), and high Gamma ($F(2.430, 19.443) = 0.625$, $p = 0.625$);

7.3.3 MI Task Block

EEG Rhythms: The mean EEG rhythms during the MI task block followed a very similar trend as in the calibration block [Figure 7.3(b)], being both blocks significantly correlated for Alpha ($r = 0.564$, $p < 0.01$), Beta ($r = 0.501$, $p<0.01$), Theta ($r= 0.599$, $p<0.01$), low Gamma ($r = 0.555$, $p<0.01$), high Gamma ($r = 0.635$, $p<0.01$). The repeated measures ANOVA revealed a significant difference for Theta ($F(2.660, 21.277) = 3.520$, $p < 0.05$). Nevertheless, no statistical differences across conditions were found for Alpha ($F(2.804, 22.429) = 0.813$, $p = 0.493$), Beta ($F(2.628, 21.020) = 2.780$, $p = 0.72$), low Gamma ($F(2.434, 19.475) = 3.199$, $p = 0.055$), and high Gamma ($F(2.232, 17.860) = 3.071$, $p = 0.067$). Post hoc tests using the Bonferroni correction revealed that there is a trend for VRMP against the control condition ($p = 0.073$) but not for the rest of the pairwise comparisons. Interestingly, the mean power of the Lower Gamma frequency band was reduced for all MI conditions, showing that EEG activation during the MI task block was more similar to motor-execution than in the calibration block, and hence in accordance with the trend identified in the rest of frequency bands [Figure 7.3].

Classification Score: In contrast to the calibration block, performance score drops considerably (> 10%) for all conditions during the subsequent MI task block, showing lower performances and higher variability [Figure 7.4(b)]. Notably, for VRMP, performance dropped to Mdn = 51.29 (IQR =

6.42), for VR to Mdn = 53.61 (IQR=12.99) and in Control condition to Mdn = 50.1 (IQR = 7.23).

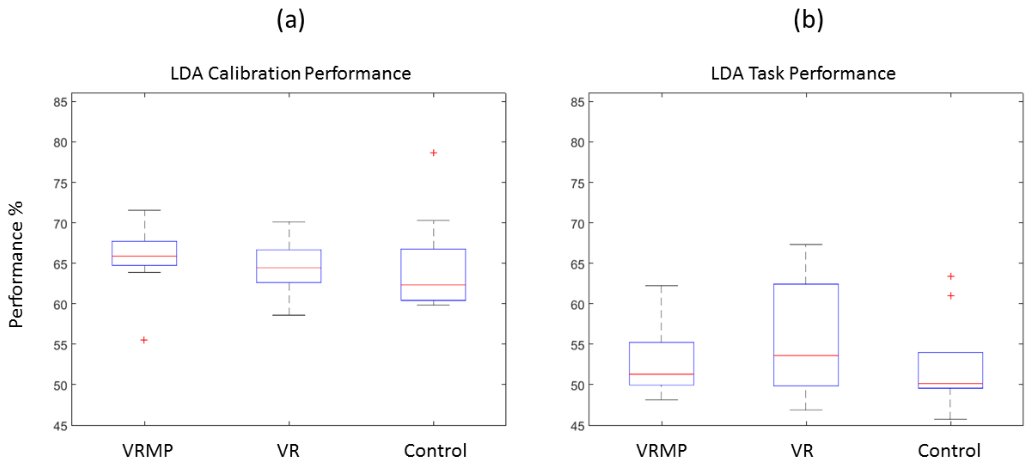

Figure 7.4: LDA classifier score. (a) Calibration score of the LDA classifier illustrating the ability of the classifier to distinguish the left — right imaginative hand movement. (b) Online task score, illustrating the ability of the classifier to distinguish the two classes with untrained data.

Hemispheric Asymmetry: A repeated measures ANOVA determined that mean difference of hemispheric asymmetry was not statistically different between conditions for the MI task, Alpha ($F(2.094, 16.754) = 1.210$, $p = 0.325$), Beta ($F(2.236, 17.891) = 1.519$, $p = 0.245$), Theta ($F(1.878, 15.023) = 1.263$, $p = 0.309$), low Gamma ($F(2.299, 18.393) = 1.047$, $p = 0.380$), and high Gamma ($F(2.287, 18.296) = 1.086$, $p = 0.366$) [Figure 7.5(b)].

7.3.4 Quality of the Experience

In order to understand how different MI training paradigms may affect the quality of the experience and the overall acceptance of the system, we analyzed a set of subjective data as reported by the participants, including the

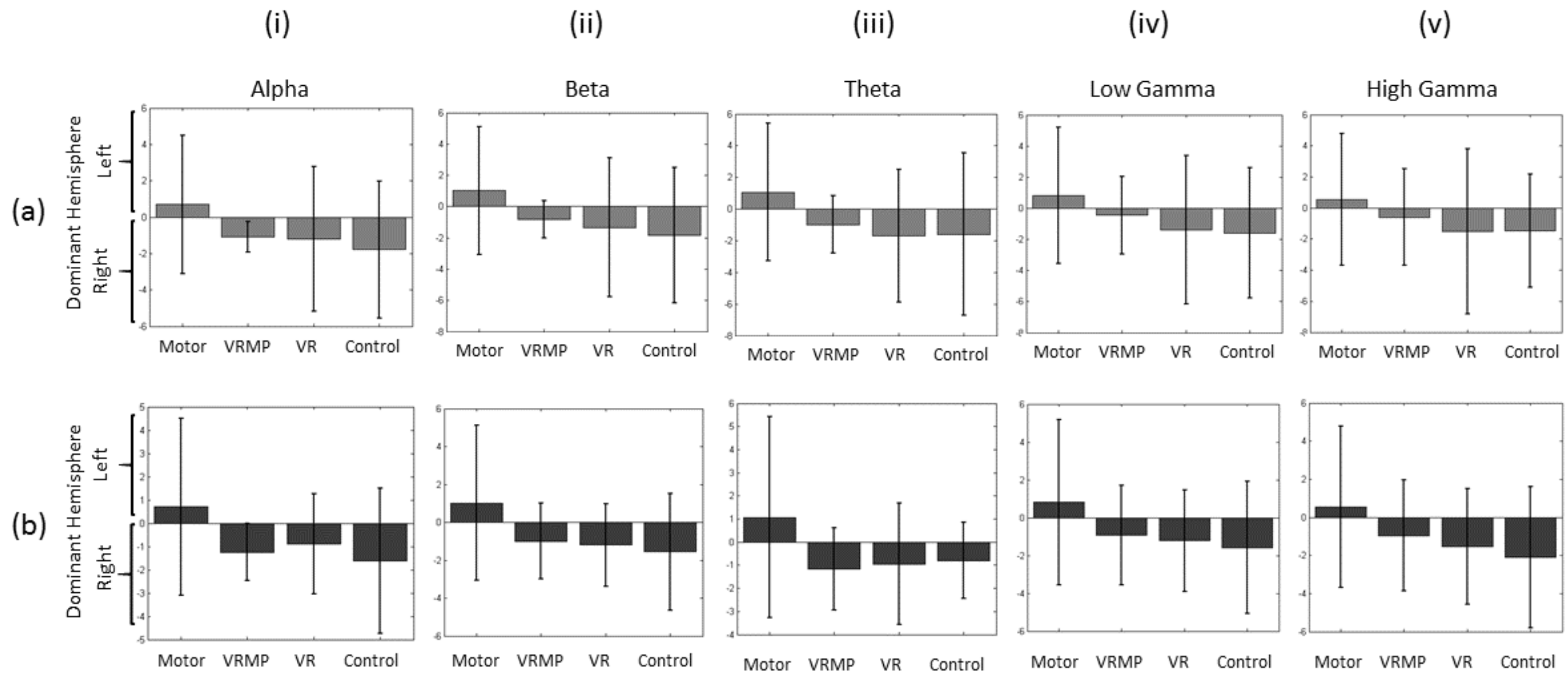

Figure 7.5: Hemispheric Differences between Left and Right EEG activation. (a) Hemispheric differences of the EEG rhythms during calibration. (b) Hemispheric differences of the EEG bands during MI task performance.

sense of Presence, Kinesthetic Imagery ability, and perceived Workload for each condition.

a) Realism of the VR Training Simulation Both VRMP and VR conditions share the same virtual environment for which users were asked to report their sense of presence. The normalized score of the Presence Questionnaire (PQ) indicates an overall acceptance of the VR task (M = 94.3%, SD = 8.3) (Figure 7.6). Overall, four out of the five domains considered scored above 70%: realism (M=73%, SD=8), the possibility to act through initiated actions and events (M=77%, SD=14), sounds of the VR task (M=79%, SD=12), and the self-evaluation of performance, which had the highest score (M=83%, SD=9). The quality of the interface showed the lowest score (M=58%, SD=13). Nevertheless, the quality of the interface did not seem to affect the high perceived performance and realism of the VR task.

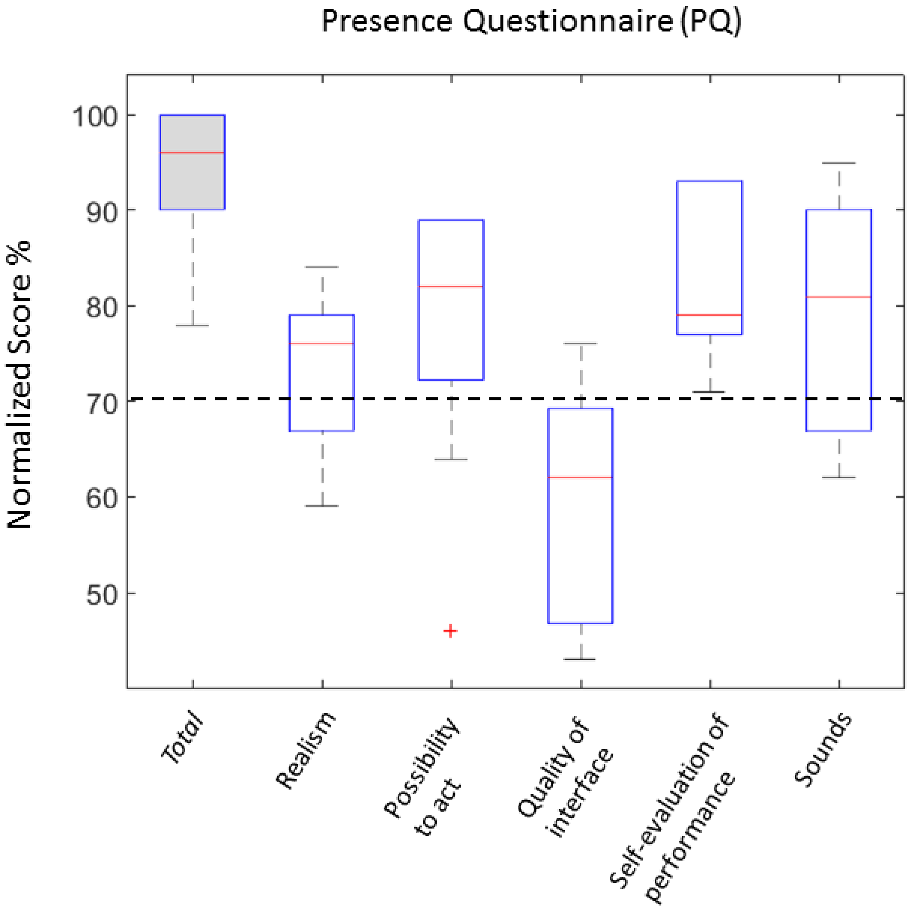

Figure 7.6: Presence Questionnaire normalized total score (gray) and the sub-domains. Four out of the five domains scored above 70%, with quality of the interface to score the lowest.

b) Correlates of Workload, Kinesthetic Imagery and Task Engagement After the MI task block on each condition, the perceived Workload was assessed through the NASA TLX questionnaire and the Kinesthetic Imagery ability through the VMIQ-2 questionnaire. A repeated measures ANOVA determined that mean Workload differed significantly across conditions ($F(1.505, 12.036) = 5.290$, $P < 0.05$) (Figure 7.7). Post hoc tests revealed that Workload in the VRMP condition to be significantly higher than for Control. A correlation analysis revealed no correlation between Workload and the performance during the MI task block.

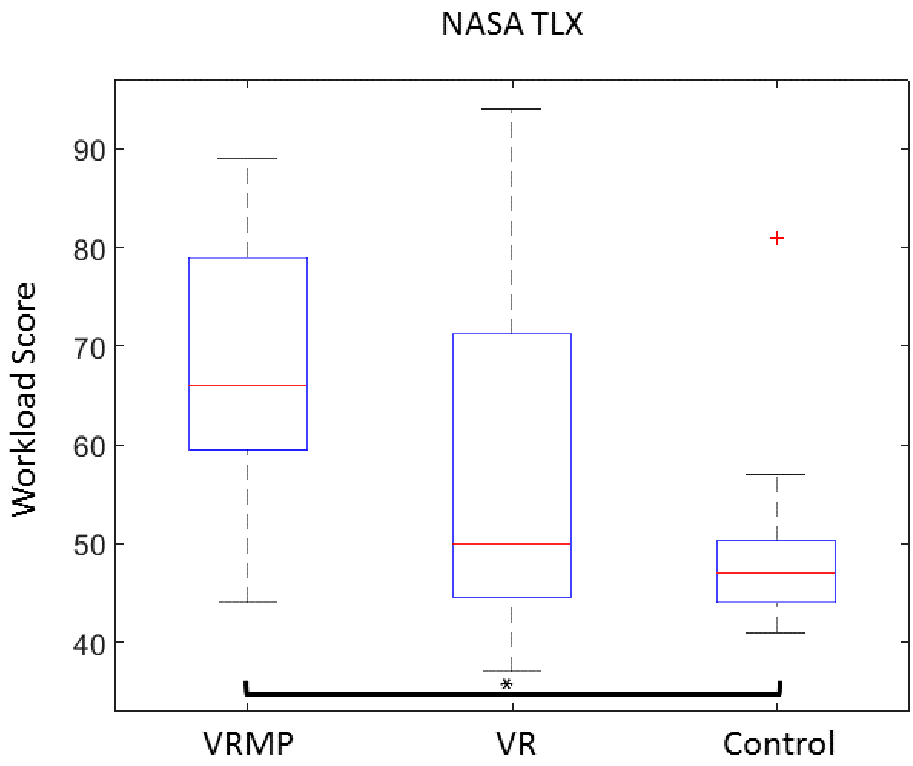

Figure 7.7: NASA TLX questionnaire for perceived Workload. VRMP condition is the most demanding in terms of task workload.

Kinesthetic Imagery was assessed through the VMIQ-2 questionnaire. The cut-off-point established by Whetstone estimates good imagery ability with a total score of 70 % [Whetstone, 1995]. Our experiment considered only first-time user experiences, and the average ability score was 61.36% (SD = 12) and only 3 out of 9 subjects scored above 70%. A comparison among conditions showed that conditions did not affect the participant's ability to create clear and vivid motor imagery ($F(1.567, 12.532) = 1.292$, $p = 0.300$) (Figure 7.8). A correlation analysis showed no significant correlation between

Kinesthetic Imagery and the performance during the MI task block.

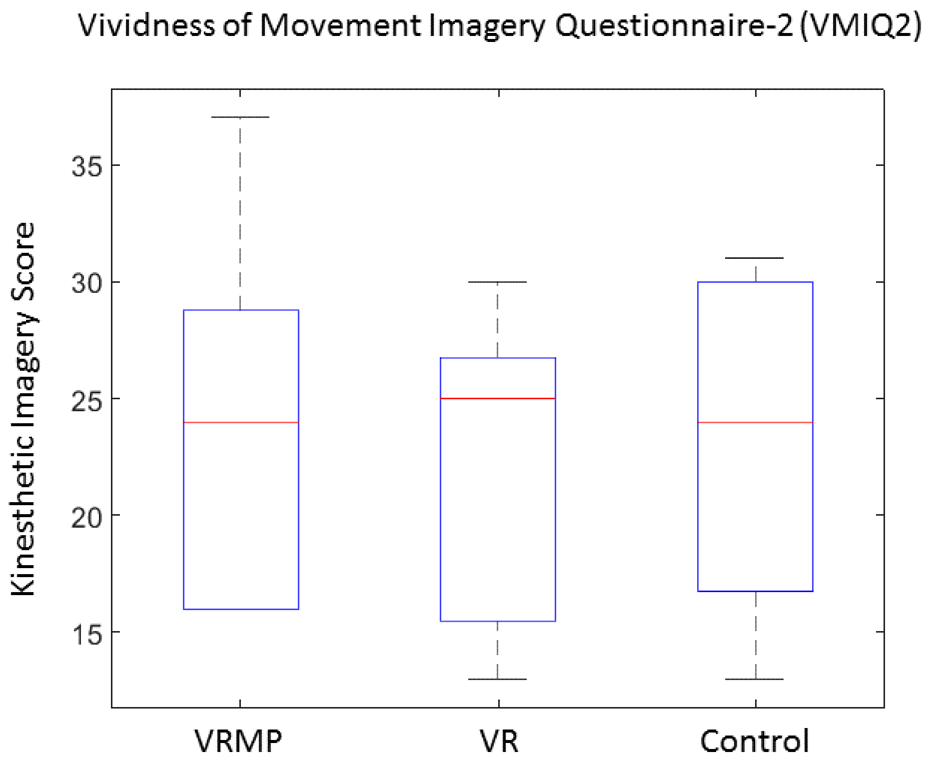

Figure 7.8: Kinesthetic Imagery (KI) score through the Vividness of Movement Imagery Questionnaire-2 (VMIQ2). Through all conditions, users had a consistent Kinesthetic Imagery ability and was not got affected across conditions.

7.3.5 Relationship between EEG rhythms and Subjective Experience

In order to identify which patient profile can benefit the most from an immersive BCI-VR setup, we investigated the relationship between subjective experience (as reported through the TLX and Kinesthetic Imagery questionnaires) and the elicited brain activity patterns (Alpha, Beta, Theta, and

Gamma EEG rhythms; and the EI). The following section illustrates the findings that have been extracted through correlation and multilinear regression modelling analyses.

a) Correlation Analysis Considering only the EEG data during the MI task block, we identified correlations of Alpha and Theta bands with the subjective reports (Table 7.1). For the TLX subcomponent of Mental Demand we found a significant correlations with Alpha ($r=0.500$, $p<0.05$) and Theta ($r=0.555$, $p<0.05$). Negative correlations were found for Alpha with the reported Kinesthetic Imagery ability in Jumping Sideways ($r=-0.381$, $p<0.05$) and Running Downhill ($r=-0.420$, $p<0.05$), and for Theta only for Running Downhill Kinesthetic Imagery ($r=-0.545$, $p<0.05$).

Table 7.1: Correlation table from MI task EEG data including Alpha and Theta bands with TLX and its subdomains.

	TLX - Mental Demand	KI - Jump Sideways	KI - Run Downhill
Alpha	0.500	-0.381	-0.420
Theta	0.555	-	-0.545

b) Multilinear Regression Modelling A stepwise regression modelling was used to identify electrophysiological predictors of subjective experience based on EEG PSD and questionnaire data (Table 7.2). Mental Demand was found to relate to a combination of Theta and Beta bands ($F(2, 24) = 8.894$, $p < 0.05$, $R2 = 0.426$). Interestingly, although both Alpha and Theta bands were shown to positively correlate with Mental Demand, this is better explained through Beta and Theta. This may indicate collinearity between Alpha and Theta bands. For Kinesthetic Imagery, Alpha band modulation is related to the user's capacity for mental imagery that involves sideways jumps ($F(1, 25) = 4.607$, $p < 0.05$, $R2 = 0.156$), and Beta and Theta for mental imagery that involves running downhill ($F(2, 24) = 10.606$, $p < 0.05$, $R2 = 0.469$).

Table 7.2: Stepwise model coefficients from online data. Electrophysiological predictors of Alpha, Beta, and Theta, based on their statistical significance. ($p<0.05$) between the questionnaires and their sub-domains.

	TLX - Mental Demand	KI - Jump Sideways	KI - Run Downhill
x1: Alpha	-	- 0.123	-
x2: Beta	1.638	-	0.204
x3: Theta	-1.107	-	- 0.273
R^2	0.426	0.156	0.469

7.4 Discussion

The obtained results contribute with a set of important findings in several dimensions: quantification of EEG modulation and classification through VR feedback and MP, and how those relate to perceived experience and Kinesthetic Imagery ability. These findings may be important to enhance the impact of MI-BCI in neurorehabilitation and push the state-of-the-art. Firstly, through the analysis of EEG rhythms we compared VR and VRMP conditions with (1) a standard control condition using Graz visualization and (2) actual EEG activity during overt motor-execution. Our EEG data revealed statistically significant differences of VRMP with standard feedback, suggesting the engagement of different underlying processes, more consistent with motor-execution data. The differences in Alpha and Beta with control and their similarity with the activity induced during motor-execution is of high importance for MI training in rehabilitation due to better association to cortical activation of sensorimotor areas during voluntary movement [Jeannerod and Frak, 1999, Rizzolatti and Craighero, 2004]. Furthermore, increased activity in Alpha and Theta could indicate an effect of increased cognitive and memory load in VR [Klimesch, 1999], as also shown in our study through TLX data. However, despite measurable differences in EEG activity among conditions, these did not significantly change the classification performance of the LDA used for BCI control. We also observed in our hemispheric asymmetry analysis that interhemispheric communication changed during the different MI-BCI paradigms. Previous studies have shown that the hemispheric asymmetry increases during feedback presentation compared to sessions without feedback [Neuper et al., 1999], enhances the performance of fine motor tasks and triggers changes in motor learning [Garry et al., 2004]. A recent study highlights that the left hemisphere is specialized for sequential motor organization in both left- and right-handers, suggesting an endogenous hemispheric asymmetry related to compound actions and skill representation [Serrien and Sovijärvi-Spapé, 2015]. Therefore, if interhemispheric communication can be modulated through VRMP as our data suggests, this is an important feature to be utilized in motor learning. In patient populations with affected hemispheric differences we could promote increased interhemispheric interaction by balancing the activation of motor-areas and influence motor performance [Takeuchi et al., 2012]. In addition, interhemispheric interactions may also contribute to intermanual transfer, as it has been found that motor learning using one hand improves the performance of the other hand [Grafton et al., 2002, Vaid and Stiles-Davis, 1989]. Therefore, longitudinal neuroimaging and electrophysiological studies are necessary in order to demonstrate the dynamic change in interhemispheric interaction between both hemispheres during the process of functional recovery in stroke survivors. Secondly, subjective data reported through questionnaires allowed us to report on their relationship with EEG data, providing insights of the effect of different MI conditions in both of cognitive and motor processes. Interestingly, although in the VRMP condition the user had to exert more physical activity, our data revealed that Physical Demand and Effort subcomponents of the TLX were not affected. We argue that the inclusion of the MP component within an immersive VR environment turned the MI-BCI task into a more mentally demanding task, with the potential of engaging more neural circuits than in the other 2 conditions. This hypothesis is also supported by the differences found in the EEG activity patterns. Additionally, we found a correlation between Kinesthetic Imagery ability and their capacity to display enhanced activity in the Alpha and Beta bands, which are modulated during cortical activation/deactivation in the planning of voluntary movement [Pfurtscheller and Lopes da Silva, 1999, Pfurtscheller and Berghold, 1989]. Finally, enhanced sensory-motor rhythms through MI-BCI training have been shown in patients displaying higher motor improvements as assessed by the Fugl-Mayer [Pichiorri et al., 2015]. Thus, our findings give further support to the importance of the vividness of motor-imagery capability in MI-BCI training, -especially the walking components of the questionnaire (jump, run)-, enabling us to use them as inclusion criteria in a neurorehabilitation MI-BCI paradigm, considering that their reliability has been assessed in both healthy and post-stroke people [Malouin et al., 2007].

7.5 Conclusions

Our findings are aligned with previous research, verifying that abstract feedback versus realistic, can have very little effect in terms of BCI classification performance, but showing that BCI feedback clearly modulates sensorimotor EEG rhythms [Neuper et al., 2009]. This could lead towards better functional outcomes compared with standard MI as reported by previous research [Pichiorri et al., 2015]. Our current results are based on the premise that it is possible to modify EEG rhythms through multimodal feedback, affecting the activity of somatosensory and motor areas for the better. This is a proposition for which there is limited empirical evidence so far. We found consistent performance trends related to the type of interface but also enhanced EEG rhythms modulation through immersive VR and motor priming. Overall, we showed that, both VR conditions elicited an increase of mean power in all EEG rhythms. Although it is known that motor-imagery involves to a large extent the same cortical areas that are activated during actual motor preparation and execution [Jeannerod and Frak, 1999], we have shown that motor-imagery training in a multimodal setup and priming (VRMP) can provide the strongest and most similar motor network activation to overt movement-execution from all tested MI-BCI training paradigms. Furthermore, the activation of ipsilateral (contralesional) primary sensorimotor cortex (SMC) and the mirror neuron system (MNS) appears to play a fundamental role in both action execution and imitation [Rizzolatti and Craighero, 2004, Hamzei et al., 2012, Michielsen et al., 2011] enhanced by VR. With current findings in hemispheric asymmetry, we can distinguish the important role of inter-hemispheric communication in motor learning. Moreover, by assessing the quality of the experience, we observed a high overall acceptance of the novel multimodal MI paradigms, despite a reported increase in Workload. By modeling electrophysiological data and perceived experience data, we are able to better describe the relationship between user profile (Kinesthetic Imagery ability, perceived Workload, Presence in VR) and EEG rhythms changes in response to MI-BCI training, which may become very relevant to identify which patients can benefit the most from it. In practice, satisfactory BCI control depends largely on the degree to which neural activity can be voluntarily controlled by users. Therefore, approaches to the training of users to control a BCI taking into consideration the specific target population play an important role. In the case of stroke survivors, our approach is based on the priming of the sensorimotor system, through realistic VR and training through gamified tasks. For patients with severe hand paresis for who motor priming through movements of the paretic limb is not possible, a VR setup such as ours could offer the ability to mirror the healthy arm during the priming session, with the affected. Mirror therapy is the use of visual illusion created by a mirror by superimposing the intact arm over the paretic. Mirror therapy is well established in stroke rehabilitation for promoting recovery [Yavuzer et al., 2008, Dohle et al., 2009]. Therefore, our system could also be used to provide MI driven mirror therapy by mirroring the healthy arm to virtual limbs. Overall, in this study we showed that MI training with multimodal setup and priming (VRMP) is an effective paradigm to elicit sensorimotor activation consistent with motor execution. We showed that thanks to our quantification of the perceived experience in MI-VR training could improve adherence to the treatment by adjusting the VR task to improve the experience. Finally, the proposed VRMP paradigm has a large potential even in the case of patients with no motor control, by exploring the possibilities of MI-BCI driven mirror therapy.

Chapter 8

Development and Evaluation of a Gamified BCI-VR Paradigm for Stroke Rehabilitation using Multimodal Stimulation

8.1 Introduction

The fusion of BCI and VR (BCI-VR) allows a wide range of experiences where participants can control various aspects of their environment -either in an explicit or implicit manner-, by using mental imagery alone [Friedman, 2015]. This direct brain-to-VR communication can induce illusions mostly relying on the sensorimotor contingencies between perception and action [Slater, 2009]. The idea of utilising BCIs in virtual rehabilitation (virtual reality and tele-medicine for neurorehabilitation), was fostered in order to complement current VR rehabilitation strategies [Bermúdez i Badia and Cameirão, 2012, Lange et al., 2012] where patients with low level of motor control –such as those suffering of flaccidity or increased levels of spasticity [Trompetto et al., 2014]- could not benefit due to low range of motion, pain, fatigue, etc. The main challenge in the use of BCIs, regardless of the BCI cost, lies in the lack of reliability and good performance at the system level that inexperienced users have [Vourvopoulos and Bermudez I Badia, 2016] due to BCI "illiteracy" of users (inability of the user to produce vivid mental images of movement resulting in poor BCI performance) [Allison and Neuper, 2010, Vidaurre and Blankertz, 2009]. Although previous studies have shown mixed results, the combination of haptic and visual feedback seems to increase the performance [Gomez-Rodriguez et al., 2011, Hinterberger et al., 2004]. It has been shown that replacing the standard visual BCI feedback with vibrotactile feedback does not interfere with the EEG signal acquisition [Leeb et al., 2013] and also does not impact negatively the classification performance [Cincotti et al., 2007, Leeb et al., 2013]. On the other hand, it has been shown to have a positive effect on visual workload measured in a multiple object tracking task (MOT) where the data revealed significant differences between visual or tactile feedback [Gwak et al., 2014]. It has also been shown that with the use of haptic feedback, the user cam pay more attention to the task instead of to the feedback [Cincotti et al., 2007], and in [Jeunet et al., 2015b] users achieved higher scores in the vibrotactile feedback setting. Vibrotactile feedback has also been used in a hybrid BCI system [Yao et al., 2014], where MI with selective sensation (SS) were used in order to increase performance. On this system, equal vibration is applied to both wrists of the user and he/she has to imagine that the vibration to one of the sides is stronger than the other (SS). SS combined with MI increased the overall performance of the system. In [Jeunet et al., 2015b], it is also reported that the vibrotactile feedback applied on the user's hand significantly increases MI performance.

In [Leonardis et al., 2012] the use of vibrotactile feedback directly applied to certain tendons is used to convey the illusion of movement to the user, and in conjunction with a virtual representation of the arm, significantly increased the accuracy of a BCI system.

Further, recent findings with the use of virtual arms have shown that the combination of motor priming (physical rehearsal of a movement) preceding BCI-VR MI training can improve performance as well as the capacity to modulate and enhance sensorimotor brain activity rhythms, important in rehabilitation research [Vourvopoulos et al., 2015a].

There is an increased need for alternative motivational mechanisms and feedback approaches for BCI systems [Lotte, 2012, Lotte et al., 2013b]. Previous research in learning, states that a poorly designed feedback can actually deteriorate motivation and impede successful learning [Shute, 2008] while providing extensive feedback to the user can lead to efficient and high quality learning [Hattie and Timperley, 2007]. Lotte et al. recommended a set of guidelines for a good instructional design in BCI training, in which (1) the user should only be presented with the correct classified action for enhancing the feeling of competence; (2) provide a simplified and intuitive task; (3) meaningful and self-explanatory task; (4) challenging but achievable, with feedback on progress of achievement; and finally (5) in an engaging 3D virtual environment [Lotte et al., 2013b].

To date, and to the best of our knowledge, there is not a holistic approach in BCI MI training that combines the advantages of different feedback modalities (immersive VR environment, vibrotactile feedback), training aproaches (motor priming preceding motor observation) and motivational mechanisms (game-like tasks).

The purpose of this study is twofold. First we describe the development and pilot assessment of NeuRow [Vourvopoulos et al., 2016b], a novel VR environment for MI training. Secondly, we present the integration with and assessment of the Adaptive Performance Engine (APE) [Ferreira et al., 2015]. The combination of APE with NeuRow is an attempt to optimize user control in a self-paced BCI-VR paradigm. NeuRow makes use of multi-modal feedback (auditory, haptic and visual) in a VR environment delivered through an immersive Head Mounted Display (HMD), integrated in a BCI MI training task (left — right hand motor imagery). Current results are presented through two studies. (1) Development and assessment of the NeuRow VR setup in terms of performance and feedback, and (2) assessment of use performance in NeuRow integrated with APE in terms of sense of control.

8.2 Experimental Setup

The experimental setup was composed by a desktop computer (OS: Windows 8.1, CPU: Intel® Core^{TM} i5-2400 at 3.10 GHz, RAM: 4GB DDR3 1600MHz, Graphics: AMD Radeon HD 6700), running the acquisition software, the BCI-VR task, HMD, EEG system, and the vibrotactile module.

EEG Acquisition: The BCI system consisted of 8 active electrodes equipped with a low-noise biosignal amplifier and a 16-bit A/D converter at 256 Hz (g.MOBIlab+ biosignal amplifier, g.tec, Graz, Austria). The spatial distribution of the electrodes followed the 10-20 system configuration [Klem et al., 1999] with the following electrodes over the somatosensory and motor areas: Frontal-Central (FC5, FC6), Central (C1, C2, C3, C4), and Central-Parietal (CP5, CP6) (Figure 8.1 a). The BCI system was connected via bluetooth to the dedicated desktop computer for the EEG signal acquisition. EEG data acquisition and processing was performed through the OpenVibe platform [Renard et al., 2010] combined with the Reh@Panel (RehabNet Control Panel) [Vourvopoulos et al., 2013] via the VRPN protocol [Taylor et al., 2001] to control the virtual environment. The Reh@Panel is a free tool that acts as a middleware between multiple interfaces and virtual environments. Feedback Presentation. For delivering feedback to the user, the Oculus Rift DK1 HMD was used (Oculus VR, Irvine, California, USA). The HMD is made of one 7" 1280x800 60 Hz LCD display (640x800 resolution per eye), one aspheric acrylic lens per eye, 110^o Field of View (FOV), internal tracking through a gyroscope, accelerometer, and magnetometer, with a tracking frequency of 1000Hz (Figure 8.1 c).

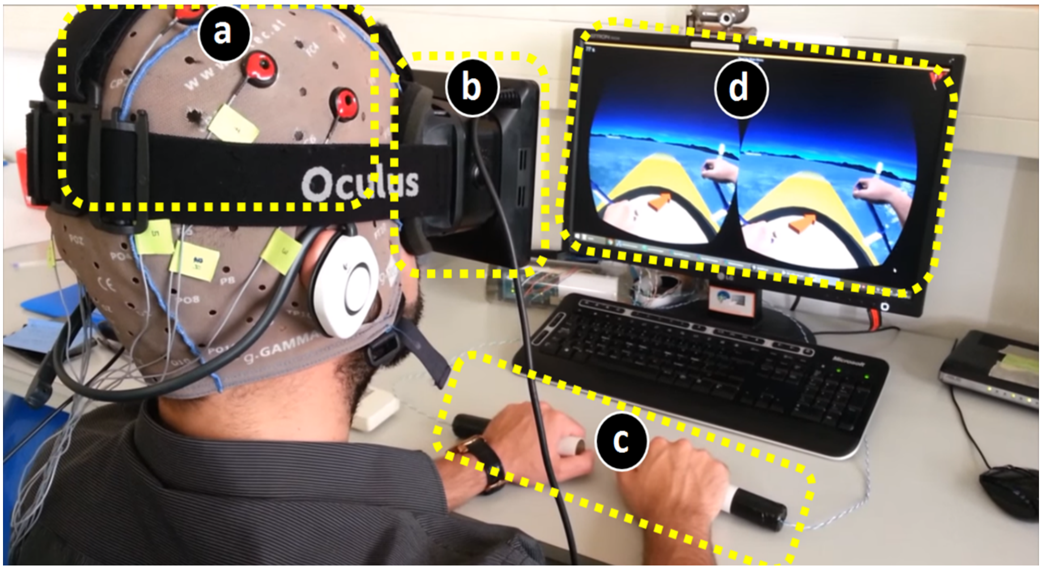

Figure 8.1: Experimental setup. (a) EEG cap with 8 active electrodes, (b) HMD, (c) vibrotactile modules, (d) BCI feedback.

Vibrotactile Feedback: A custom vibrotactile feedback module was developed with out-of-the-box components including an Arduino Mega 2560 board and vibrating motors. The vibrating motors (10mm diameter, 2.7mm thick) performed at 11000 RPM at 5V and were mounted on cylindrical tubes that acted as grasping objects for inducing the illusion of movement during the BCI task (Figure 8.2 c). In our setup, a pair of cardboard-based tubes with 12cm of length and 3cm diameter were used. Finally, 3D printed cases were produced to accommodate the vibrating motors inside the tubes (Figure 8.2). All hardware and software blueprints are made available free online[1].

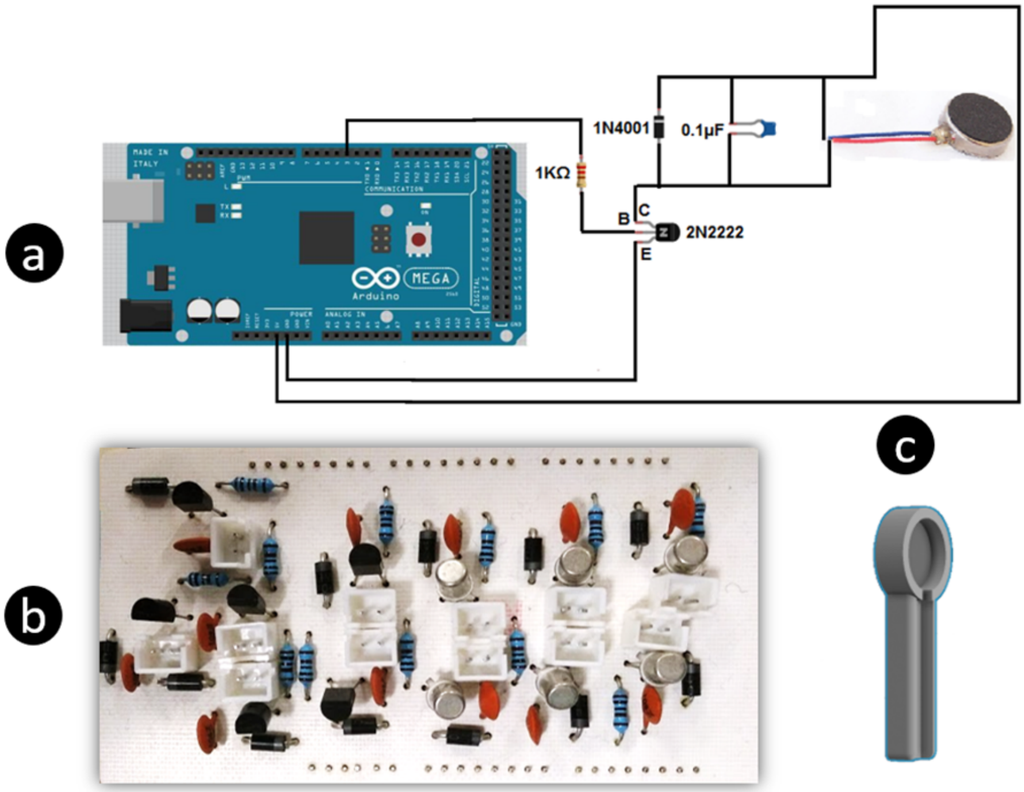

Figure 8.2: Custom vibrotactile module.(a) Arduino board schematic including the necessary electronic components (for one motor), (b) custom Arduino shield, (c) 3D printed casing for motors.

[1] http://neurorehabilitation.m-iti.org/bci/neurow/vibrotactile-module/

8.3 BCI Task Design

BCI-VR Training Protocol: The training protocol was designed and adapted based on the Graz-BCI paradigm [Pfurtscheller et al., 2003], substituting the standard feedback presented (directional arrows) by multimodal VR feedback. The first step of the training consisted on the acquisition of the raw EEG data to train a linear discriminant classifier to distinguish Right and Left imagined hand movements. Throughout the training session, the user performs mental imagery of the corresponding hand (based on the presented stimuli). For each hand, the user is stimulated visually (VR action observation), auditorily, and haptically through the vibration on the corresponding hand (Figure 8.3 a). The training session was configured to acquire data in 24 blocks (epochs) per class (Right or Left hand imagery) in a randomized order. Following the training, data are used to compute a Common Spatial Patterns (CSP) filter, a spatial filter that maximizes the difference between the signals of the two classes. Finally, the raw EEG and the spatial filter are used to train a Linear Discriminant Analysis (LDA) classifier.

BCI-VR Task: The BCI-VR task was designed based on literature and previous work, incorporating important features for a successful brain-to-computer interaction in terms of feedback, protocol design, and accessibility [Lotte, 2012]. The BCI-VR task involves boat rowing through mental imagery only with the goal of collecting as many flags as possible in a fixed amount of time. NeuRow is a self-paced BCI neurogame, meaning that is not event related, and the user controls the timing of rowing actions like he/she would do in real-life (Figure 8.3 b).

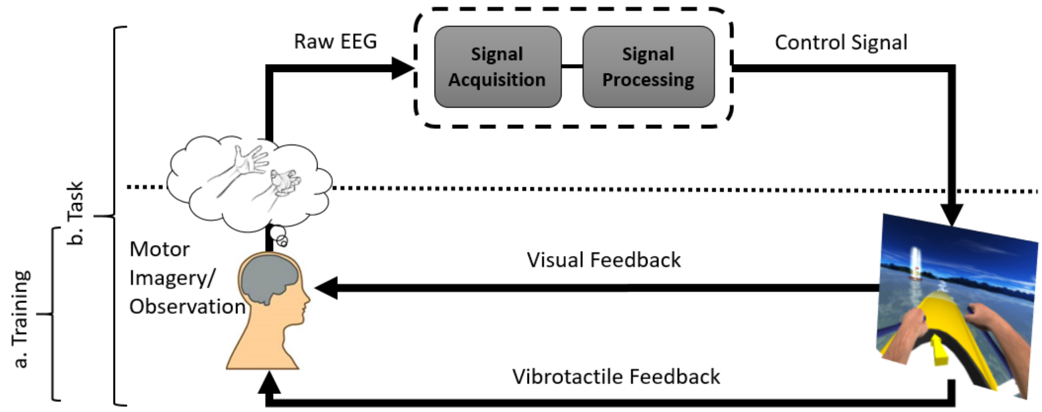

Figure 8.3: Neurofeedback loop. (a) During the training session, the user is performing in a randomized order MI combined with motor observation of the virtual hands rowing while vibrotactile feedback is delivered to the corresponding hand. (b) The user relies on MI alone in order to control the virtual hands in a closed-loop system after training

8.4 Implementation

NeuRow is a multiplatform virtual environment developed in Unity game engine (Unity Technologies, San Francisco, California, USA). Finally, NeuRow is optimized for different platforms, however with different features (Table 8.1). Namely:

- **Desktop:** The standalone version for PC, supports immersive VR experience with the support of the Oculus Rift DK1 headset, HTC Vive the Leap Motion hand controller available for optional motor-priming before the MI BCI session. Finally, vibrotactile feedback is supported through the use of custom made hardware for controlling through USB up to 6 vibration motors. Data logging is supported for boat trajectory, target location, score and time.

- **Mobile:** The mobile version is designed for Android devices, receiving data via the RehabNet UDP protocol. For phones, the VR feature is utilized for VR glasses (e.g. Google VR) by applying lens correction for each eye, and using the phone gyroscope and magnetometer for tracking head rotation, offering experience similar to the Oculus DK1 HMDs

- **Web browser:** The web version uses the Unity web player (compatible through Internet Explorer, Firefox or Opera), does not support the networking, HMD and haptic components due to security restrictions. Instead, the web NeuRow acquires data through emulated keyboard events generated by the Reh@panel.

Table 8.1: NeuRow features for the different supported platforms.

Features/ Platform	**Desktop**	**Android**	**Web**
Logging	✓	X	X
VR	✓ (Oculus, HTC Vive)	✓ (Google VR)	X
Hand Tracking	✓ (Leap Motion)	X	X
Networking	✓	✓	X
Platform Independent	X	X	✓
Vibrotactile Feedback	✓ (Arduino)	X	X

In-game, two high fidelity virtual arms are rendered together with time indication, score and navigational aids (Figure 8.4). NeuRow can be customized with different settings. One can chose if the session is part of the MI training or self-paced online control of the boat. During training, the navigational arrow and the targets are removed to focus the user only on the multimodal MI BCI-VR task. During self-paced mode, the behavior of the boat can be changed by setting the heading speed, turn speed and cut-off angle. The cut-off angle is the allowed angle that the boat can be off-course with respect to the target flag before stopping. This serves as a protection mechanism to help the player not to deviate from the target.

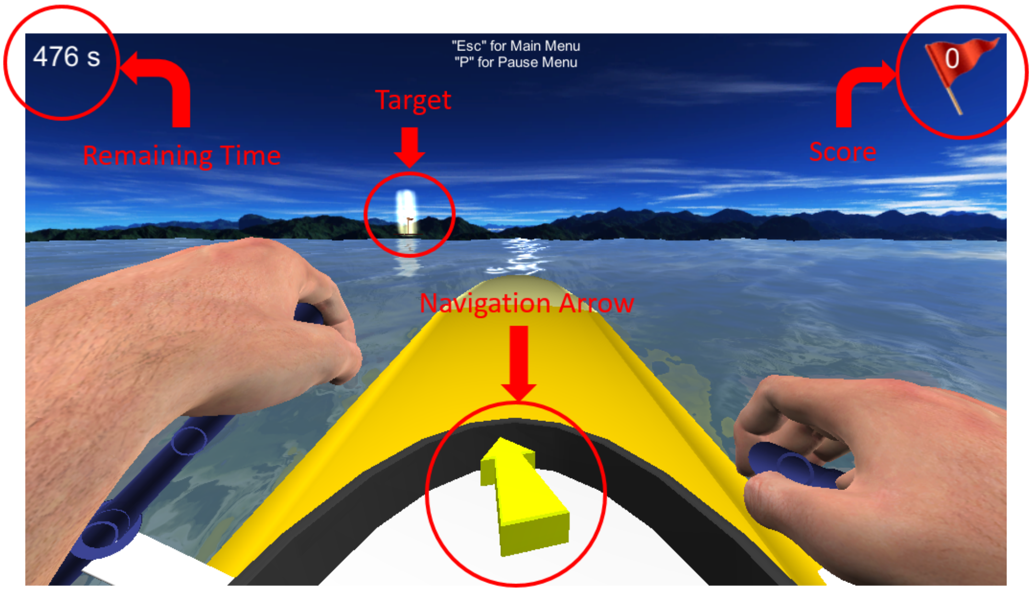

Figure 8.4: In-game interface. An arrow indicates the direction of the target and also the distance by changing its color (red for far blending up to green for close). Top Left: Remaining time for the end of the session. Middle: A flag with a ray acts as the game targets, Top Right: Game scoring, counting the number of targets.

8.5 Participants

A voluntary sample of 13 users (mean age of 28 ± 5 years old) was recruited for the study, based on their motivation to participate in the study. All participants were male and right handed with no previous known neurological disorder, nor previous experience in BCIs. Participants were either university students or academic staff. Finally, all participants provided their written informed consent before participating in the study.

8.6 Questionnaires

Before each BCI training session, demographics and user data were gathered through the following questionnaires:

- The Vividness of Movement Imagery Questionnaire-2 (VMIQ2) was used to assess the capability of the participant to perform an imagined movement (Kinesthetic Imagery) [Roberts et al., 2008]. Kinesthetic Imagery (KI) questions were combined with mental chronometry by measuring the response time in perceptual-motor tasks with the help of a timer.

- For assessing gaming experience we used the Gamer Dedication (GD) questionnaire, a 15 factor classification questionnaire in which participants are asked whether they "strongly disagree," or "strongly agree" with a series of statements about their gaming habits [Adams and Ip, 2002].

After the BCI task, the following questionnaires were administered:

- The NASA TLX questionnaire was used to measure task load considering Mental Demand, Physical Demand, Temporal Demand, Performance, Effort and Frustration [Hart and Staveland, 1988].
- The core modules of the Game Experience Questionnaire (GEQ) were used at the end of the BCI session. GEQ assesses game experience using Immersion, Flow, Competence, Positive and Negative Affect, Tension, and Challenge [IJsselsteijn et al., 2008].
- The System Usability Scale (SUS) is a ten-item scale giving a global view of subjective assessments of usability [Brooke, 1996].

8.7 EEG Data Analysis

Power Spectral Density (PSD): EEG signals were processed in Matlab (MathWorks Inc., Massachusetts, US) with the EEGLAB toolbox (Delorme and Makeig, 2004) for extracting the Power Spectral Density (PSD). The power spectrum was extracted for the following frequency rhythms: Alpha (8 Hz - 12 Hz), Beta (12 Hz - 30 Hz), Theta (4 Hz - 7 Hz), and Gamma (25 Hz - 90 Hz). Independent Component Analysis (ICA) was used for removing major artefacts related with power-line noise, eye blinking, ECG and EMG activity. For the current analysis, and because we were only measuring from sensory-motor areas, data were averaged for all the channels for each experimental condition.

Engagement Index: The Engagement Index (EI) was computed from the EEG bands, according to the EI formula (*Beta/(Alpha+Theta)*), as mentioned in previous chapters. EI is a metric proposed at NASA Langley for evaluating operator engagement in automated tasks, was validated through a bio-cybernetic system for Adaptive Automation [Pope et al., 1995], and is widely used in EEG studies for assessing engagement [Berka et al., 2007].

8.8 Results

In the following section we analyse NeuRow's BCI task performance in terms of classifier score during training, user acceptance as assessed by the SUS, GEX and TLX questionnaires, and finally the relationship between game behaviour and user experience through the questionnaires and also the EEG activity.

8.8.1 Performance

Comparing the performance score with previous studies which used LDA classifiers in two class (left, right hand) MI, we are able to gain insights concerning the effectiveness of our BCI-VR paradigm in terms of user control [Boostani and Moradi, 2004, Garcia et al., 2003, Obermaier et al., 2001, Solhjoo and Moradi, 2004]. As illustrated in Figure 8.5, the comparison places NeuRow as the fourth highest with a mean performance of 70.7% out of 12 studies. Moreover, of those studies that used exactly the same feature extraction technique of band power (BP) and CSP [Vourvopoulos et al., 2015a, Vourvopoulos and Bermudez I Badia, 2016], NeuRow scores the highest. Finally, of those studies that used VR as a training environment [Vourvopoulos et al., 2015a], again NeuRow scores first.

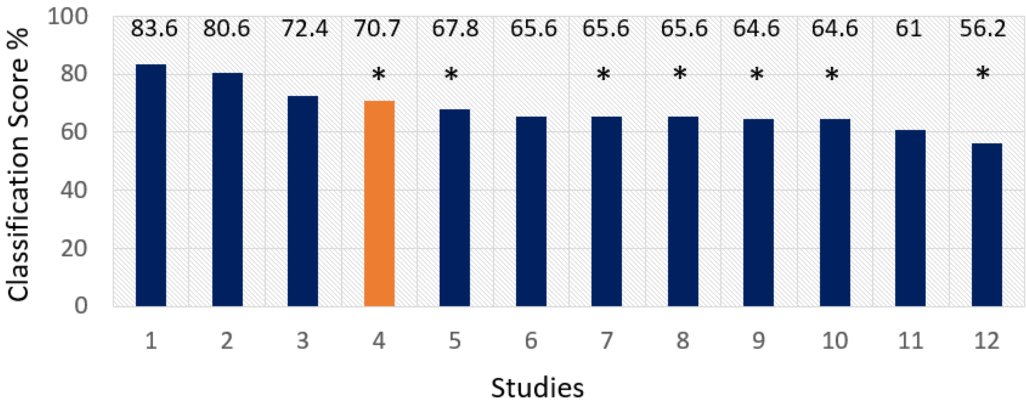

Figure 8.5: Ranked accuracy of performance in pure MI based BCI studies using two-classes (left and right hand imagery) with respect to LDA classification [Boostani and Moradi, 2004, Garcia et al., 2003, Obermaier et al., 2001, Solhjoo and Moradi, 2004]. The asterisk (*) over 4,5,7,8,9,10 and 12 [Vourvopoulos et al., 2015a, Vourvopoulos and Bermudez I Badia, 2016] indicates studies which use the same feature extraction method (BP with CSP). The data of this study corresponds to the 4th best.

8.8.2 User Acceptance

To assess different aspects of the user experience during online control of NeuRow, the mental workload, gaming experience and system usability were assessed after the task. For workload, the NASA-TLX mean score was relatively high at 66.8/100 (SD = 14.5). As it is illustrated in Figure 8.6, the two lowest scores are those for physical (M = 4.4, SD = 3.4) and temporal (M = 6.5, SD = 3) demand. The highest score is on effort (M = 16.4, SD = 5.2) followed closely by frustration (M = 13.3, SD = 5.2) and mental demand (M = 12.8, SD = 5). Performance lies in the middle (M = 11.4, SD = 6.2).

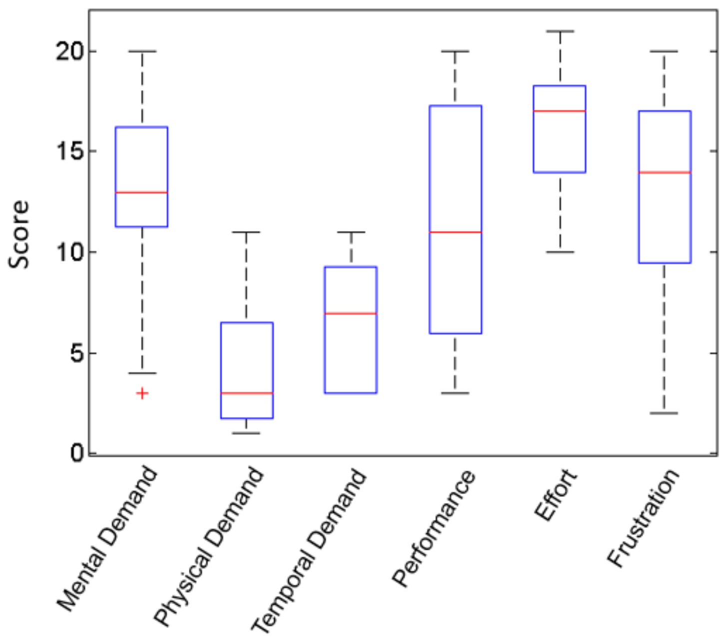

Figure 8.6: TLX scores between 1-20 for mental demand, physical demand, temporal demand, performance, effort and frustration.

From the GEQ, we extracted seven domains based on the sub-scale scoring. The highest score is in flow (M = 3.1, SD = 0.4) followed by immersion (M = 2.8, SD = 0.4) and positive affect (M = 2.8, SD = 0.7). A moderate score is achieved on tension/annoyance (M = 2.5, SD = 0.9) and challenge (M = 2.5, SD = 0.5). Finally, competence (M = 1.8, SD = 0.7) and negative affect scored the lowest (Figure 8.7). The system usability assessed by the SUS scored a mean of 74 (SD = 7.2). Based on the SUS rating scale (Figure 8.8), our system is classified as "Good" and it is within the acceptability range [Bangor et al., 2009].

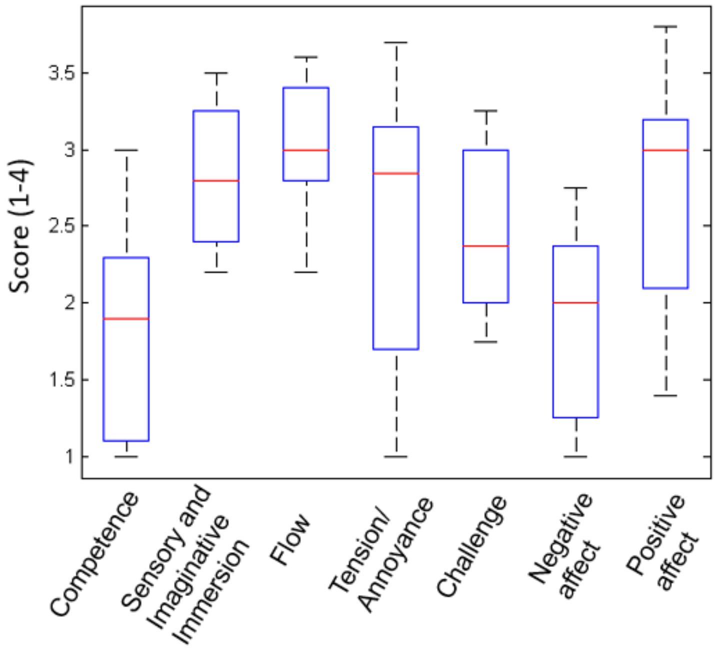

Figure 8.7: Scores for the GEQ core questionnaire domains

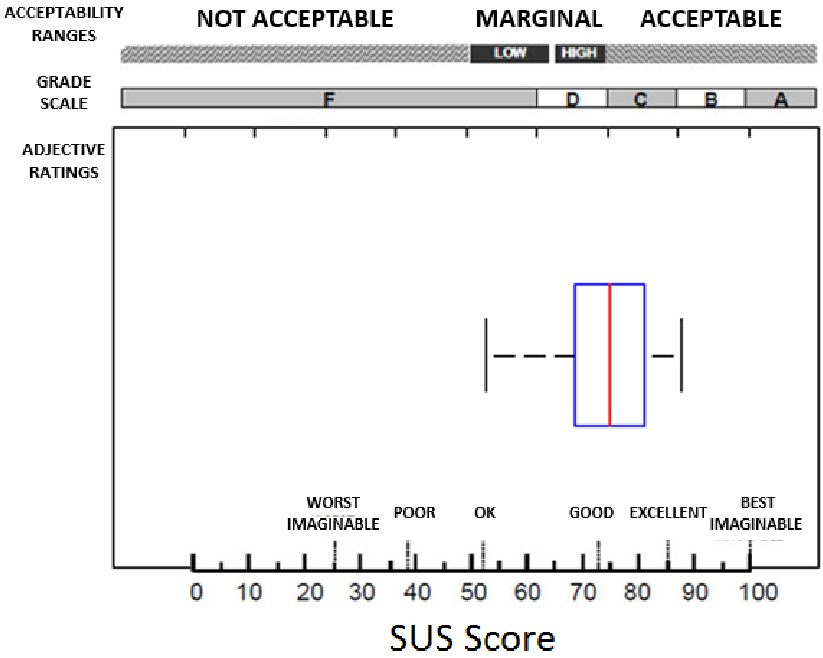

Figure 8.8: SUS results for all users. Acceptability scales are displayed on top (not acceptable, marginal and acceptable), followed by the grade scale (A to F) and the adjective rating (0-100)

8.8.3 User-Profile and in-Game Behaviour

By assessing the relationship of the reported experience and the EEG activity with the in-game behaviour (score, distance, speed, trajectory) we identified a set of correlations. As illustrated in Table 8.2, the total workload correlates with distance, speed and score. In addition, two TLX sub-domains have correlations. Performance is significantly correlated with distance and speed, as well as frustration is significantly correlated with distance, speed and score. Furthermore, mental chronometry (the response time in perceptual-motor tasks), significantly correlates with distance, speed and score. Finally, from the extracted EEG bands and the resulting Engagement Index, we can

Table 8.2: Correlation table between reported experience, extracted EEG bands and in-game behaviour.

	Distance	Speed	Score	Smoothness
TLX: Total	-.695	-.699	-.697	
TLX: Performance	-.595	-.599		
TLX: Frustration	-.728	-.737	-.686	
Mental Chronometry	.618	.615	.728	
Alpha band	-.611	-.607		
Theta band	-.672	-.670		
Engagement Index	-.770	-.768	-.649	-.595

see that Alpha and Theta bands are reversely correlated with distance and speed. Finally, Engagement Index is interestingly correlated with all in-game metrics. In particular for distance, speed, score and trajectory smoothness.

Overall, we identified an imbalance between theoretical training performance (LDA) and actual quality of the online performance (game score and control). In current MI-BCI interaction users undergo long, tiresome and complex periods of training so that EEG classification score can reach acceptable performance rates. On the follow-ing chapter, we propose to reverse the problem and make MI-BCI interaction adap-tive to the user, so that we can guarantee a satisfactory performance rates by soften-ing decisions – making them probabilistic and non-time-constrained – depending on our confidence on the user's EEG data.

8.9 Conclusions

In this study, we presented the design, development and pilot evaluation of NeuRow, a novel BCI-VR system for MI training, extended by a study about the per-ceived sense of control using APE. In terms of classification performance, the NeuRow BCI training paradigm showed higher performance, scoring the first amongst other studies with similar feature extraction and classification methodologies. These data supports a positive effect of the combination of immersive VR and vibrotactile feedback to help users to produce vivid MI (resulting in more distinct activation of sensorimotor areas of the brain), which in turn can lead to increased performance and learning [Sigrist et al., 2013]. Furthermore, from the user experience point of view, we can see high mental effort as given by the TLX scales and low physical and temporal de-mands. Previous research in distinguishing difficulty levels with brain activity measurements indicated an average mental workload index of 26 (SD = 12.9) for the easy level, and 69 (SD = 7.9) for the hard level [Girouard et al., 2009]. The combination of low physical demand (useful in low mobility patients), increased effort (a conscious exertion of power) and good classification performance (better control that can lean in goal achievement), constitutes a very promising finding for the incorporation of this technology in stroke rehabilitation, providing new possibilities for rehabilitation programs. Moreover, increased flow and immersion to the task, in combination with increased positive affect, are good elements for enjoyment of NeuRow that can be capitalized on to further motivate and engage users in their BCI training. From the correlation analysis between user experience -subjectively measured through questionnaires but also objectively measured through EEG activity- and in-game behavior, we can see that people with increased workload will perform worse. Interestingly, we can see that users with fast response time in MI ability (as extracted from the mental chronometry assessment) performed better in the game, being it then an indicator of increased capability of MI. Further, having a fast and vivid sensation of kinesthetic imagery can be related to an increased modulation of sensorimotor rhythms [Neuper et al., 2005], resulting in better BCI calibration and, hence, higher in-game performance. In addition, the reverse correlation of the Engagement Index with all the in-game variables shows an important connection between user engagement and in-game behavior. This relationship can help in developing a neurofeedback closed loop where the engagement of the user is used to adjust parameters of the game. This would allow a dynamic adjustment of the game based on user performance and cognitive state.

Chapter 9

Augmenting Control through Adaptive Performance

9.1 Introduction

Following the design and development stage of NeuRow, as a next step, we conducted a complementary assessment by incorporating the Adaptive Performance Engine (APE) module together with the Reh@Panel. APE aims at adapting the BCI interaction to each user in order to maximize the level of control on their actions, whatever their performance level is. Our objective is evaluating the improvements in performance and perceived sense of control -at the user level instead of the classifier output- with the APE. For this, we integrated a state-of-the-art HMD for increased immersion and an ultraportable wireless EEG system.

9.2 Experimental Setup

For this second study, a dedicated desktop computer was used for delivering the multimodal feedback: the VR environment, the vibrotactile module and the HMD (OS: Windows 10 Pro, CPU: Intel® Core™ i7-6700 at 3.40GHz, RAM: 8GB DDR3 1600MHz, Graphics: AMD Radeon R9 390 Series). Additionally, a second desktop (OS: Windows 10 Pro, CPU: Intel® Core™ i5-4440 at 3.10GHz, RAM: 8GB DDR3 1600MHz, Graphics: AMD Radeon R7 200 Series) was utilized for the EEG data acquisition and online processing

EEG Acquisition: For EEG acquisition, the Enobio 8 (Neuroelectrics, Barcelona, Spain) system had been used. Enobio, is a wearable, wireless EEG sensor with 8 EEG channels and a triaxial accelerometer, for the recording and visualization of 24 bit EEG data at 500 Hz. The spatial distribution of the electrodes followed the same electrode placement as the first study, over the somatosensory and motor areas: Frontal-Central (FC5, FC6), Central (C1, C2, C3, C4), and Central-Parietal (CP5, CP6). The BCI system was connected via bluetooth to the second dedicated desktop computer.

Feedback Presentation: For delivering feedback to the user, the HTC Vive HMD was used (HTC, New Taipei City, Republic of China; Valve, Kirkland, Washington, Unit-ed States) (Figure 9.1). The Vive uses two screens, one per eye, each having a display resolution of 1080x1200 and a refresh rate of 90 Hz. Additionally, the Vive uses a gyroscope, accelerometer and laser position sensors, and operates in a 4.6 x 4.6 m (15-by-15-foot) tracking space by using two "Lighthouse" base stations that track the user's movement with sub-millimeter precision. The Lighthouse system uses photo-sensors by sweeping structured light lasers within a space.

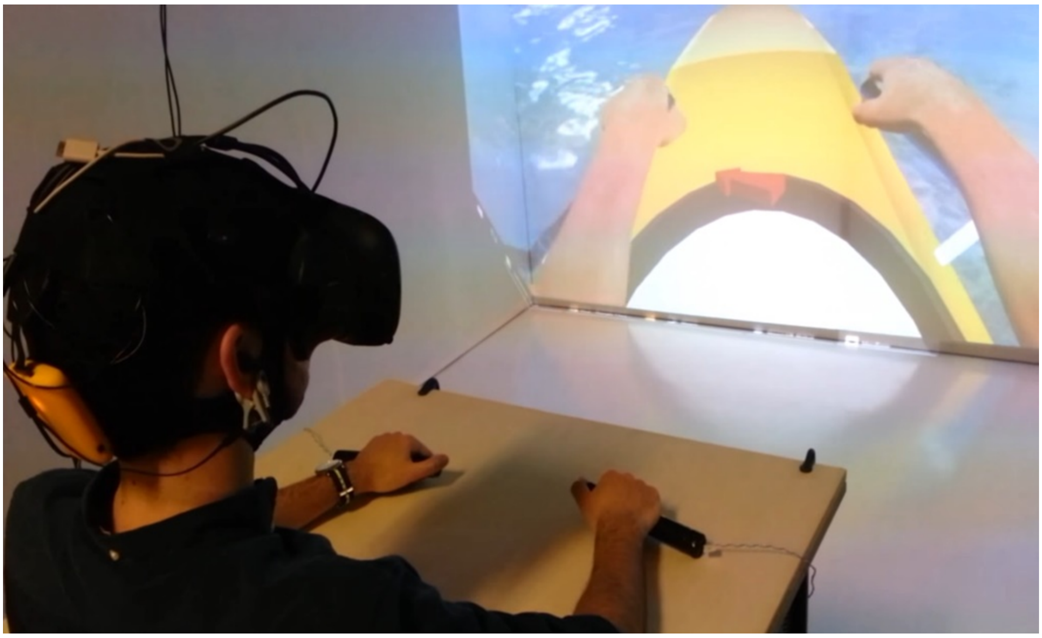

Figure 9.1: NeuRow setup including the HTC Vive HMD and Enobio 8 EEG headset (projected feedback is for illustration purposes only).

9.3 BCI Protocol

For both the training and the BCI task, an identical protocol and setup to the previous experiment were used. During training the NeuRow feedback had been displayed for left—right motor observation and motor imagery of the rowing task, delivering also vibrotactile feedback. Following training, two conditions were delivered in random order: (1) standard output of the LDA classifier, and (2) the APE (Figure 9.2).

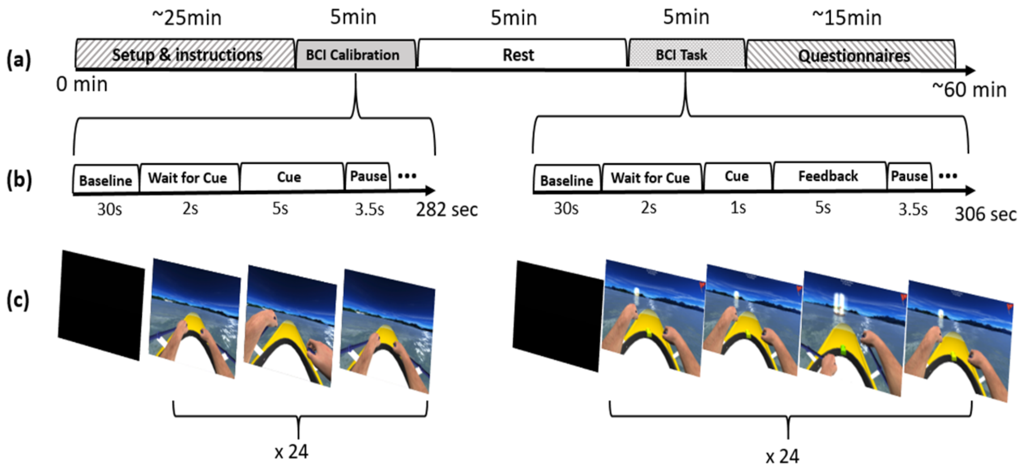

Figure 9.2: BCI protocol for training and online control

9.4 The Adaptive Performance Engine

The Adaptive Performance Engine (APE) is composed by 2 main components: (a) a Bayesian Inference Layer (BIL) a (b) Finite State Machine (FSM). The BIL was used in order to formulate the input into a model, where we translate the continuous BCI classification data into probability. BIL was chosen since it is a simple computational approach and more efficient as compared to other supervised learning techniques such as artificial neural networks. As for decision making, we made use of an FSM because of its efficiency and non-linear properties. More concretely:

Bayesian Inference Layer: BIL was designed to complement the standard Linear discriminant analysis (LDA) classifier that results from MI BCI training, and is used to compute the likelihood of the classifier output for each class (left vs. right motor-imagery). This is done by modeling the data belonging to each class as a Gaussian distribution, where μ and σ indicate their mean and standard deviation values ($MI_i(\mu, \sigma), i = [left, right]$). We then compute the Likelihood of a specific LDA output belonging to each MI class with:

$$P(i \mid LDAoutput) = \frac{MI_i(LDAoutput, \mu_i, \sigma_i) * P_i}{\sum_j MI_j(LDAoutput, \mu_j, \sigma_j)} \tag{9.1}$$

Where P_i indicates the prior probability of action i (0.5 for left vs. right MI). μ and σ are updated at each iteration, taking into account all previous history of the user for the given i MI action. LDA output indicates the output value of the LDA classifier.

Finite State Machine: Following the BIL, the likelihood of each MI classification is forwarded into a FSM. The role of the FSM is to transform binary MI classifications – such as left vs. right as given by the LDA – into evidence-based states (S_i). The FSM is composed of 7 states, a neutral (S_0) and three for each MI class ($S_{1/-1}, S_{2/-2}, S_{3/-3}$). Each state has a transition threshold associated with it (w_1, w_2, w_3), and can only transition to one of the nearest neighbors or stay in the same state (Figure 9.3). As input, the FSM uses the difference of the posterior probabilities of left and right MI from eq 9.1 and each state represents not only the class (negative and positive states represent left and right MI respectively), but also the confidence level associated to them (being $S_{3/-3}$ the most certain states).

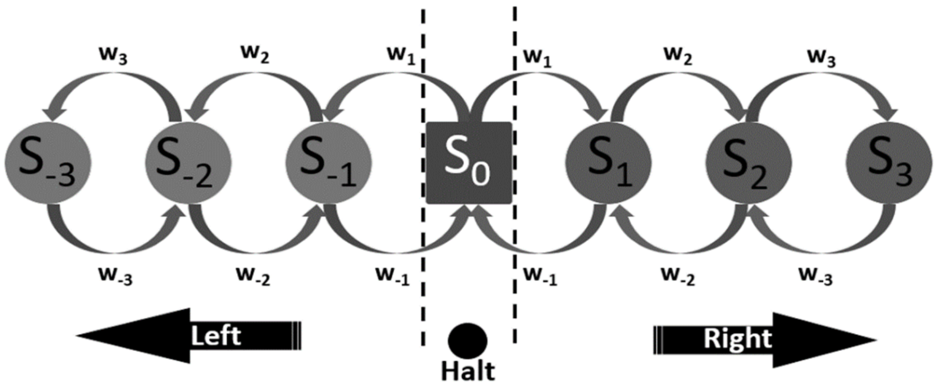

Figure 9.3: State transition diagram

Increase of Performance In order to answer if we can improve performance by means of the BCI-APE approach, we used a dataset with MI training sessions of 15 naïve users to explore the parameter space of the aforementioned state machine thresholds (W_i) from 0 up to 0.3 on a 0.05 step, what resulted in 117649 FSM parameter combinations. For each combination we quantified the percentage of indecisions (S_0) and the correctness of decisions based on the remaining states. Results show that the FSM approach can increase performance over the original LDA classification (up to ap-prox. 20%) at the expense of an increased amount of indecisions (Figure 9.4). That is, less decisions are taken but with higher confidence.

From new training data we obtained with our system, the classification performance with standard LDA was 58.70% ± 7.84%; Average improved performance of BCI-APE 70.46% ± 6.90%; Average maximum performance of BCI-APE 85.37% ± 10.09%; and indecision's of BCI-APE 48.25% ± 24.62%. Further, we implemented the complete BIL + FSM based on the above models of performance increase and we tested it against a dataset from 5 different BCI naive users containing 5x120 MI trials. The previous results are confirmed with the test data: Classification performance with standard

LDA 63.93% ± 6.28%; Average improved performance of BCI-APE 71.83% ± 6.64%; Average maximum performance of BCI-APE 88.37% ± 6.49%; and indecision's of BCI-APE 38.82% ± 19.60%.

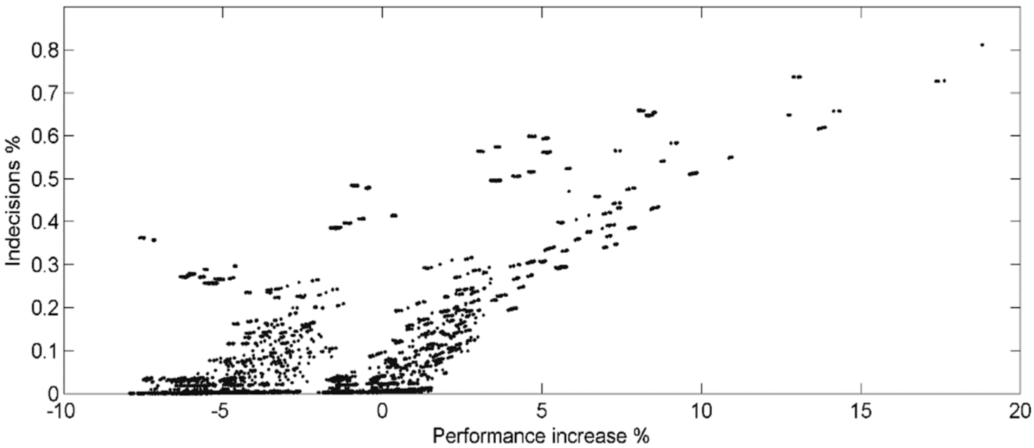

Figure 9.4: Performance increase vs. indecisions percentage for the 117649 FSM parameter combinations on a MI dataset of 15 naïve users.

9.5 Participants

For assessing the APE, a sample of 8 users (mean age of 27 ± 3.5 years old) was recruited, based on their motivation. All participants were male and right handed with no previous known neurological disorder. Four of the users had little prior experience with MI-based BCI. All participants were university students of the University of Madeira and provided their written informed consent before participating in the study.

9.6 Questionnaires and EEG data

Before each session, the Movement Imagery Questionnaire—Revised second version (MIQ-RS)) [Gregg et al., 2010] was admitted to each participant.

MIQ-RS is an 18-item questionnaire for mental imagery comprised of nine visual imagery and nine kinesthetic imagery items, each of which involves the movement of an arm, leg or the entire body. To complete each item, four steps are required: (1) The starting position for each movement is described, and the participant is initiating that position, (2) The movement is then described and the participant physically performs the movement, (3) The participant retakes the starting position, and images the movement without physically performing the movement, (4) Finally, the participant rates the ease or difficulty of imaging the movement on a 7-point scale anchored by 1 = very easy to picture/feel and 7 = very difficult to picture/feel. Following MIQ-RS, the Vividness of Movement Imagery Questionnaire-2 (VMIQ2) [Roberts et al., 2008] was used including the visual and kinesthetic parts of the questionnaire. After each session, the NASA TLX questionnaire was used to measure task load considering Mental Demand, Physical Demand, Temporal Demand, Performance, Effort and Frustration [Pope et al., 1995]. Finally, on each condition, the raw EEG data were logged in order to extract the different EEG bands and the Engagement Index derived from these bands.

9.7 Results

The main objective was to understand how to improve performance for online control. For quantifying the quality of control between the two conditions, we analyzed the in-game data (trajectory, score), perceived experience through the SOPI and TLX questionnaires, and finally, the EEG bands modulation including the Engagement Index.

Quality of Control: In terms of control, Figure 9.5 illustrates the in-game boat trajectories resulting from the Raw LDA control (blue) compared with the APE decision mechanism (orange) for the same task, subject, and with the in-game targets on the same positions. The trajectory with APE is steadier than the Raw LDA control, displaying a smoother trajectory. It is also visible in the APE trial that users could perform equally both left and right turns, while the Raw LDA trajectory is generally dominated by one dominant hemisphere, resulting in frequent rotation in one direction.

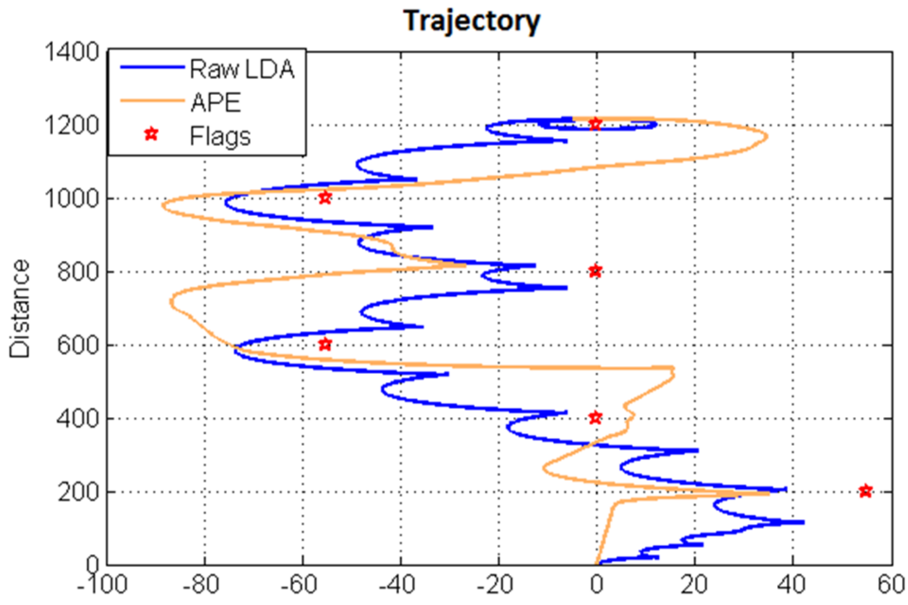

Figure 9.5: Example of in-game boat trajectory during raw LDA classification output vs APE output for subject 1

The improvement in control is also apparent by the number of sudden trajectory changes or “spins” present during navigation, being considerably higher for Raw LDA than for APE (Figure 9.6 Finally, the increased accuracy per decision of APE is reflected in an increased perceived sense of control during APE (Figure 9.6 c). Nevertheless, neither the in-game scores nor the reported sense of control differ significantly between conditions.

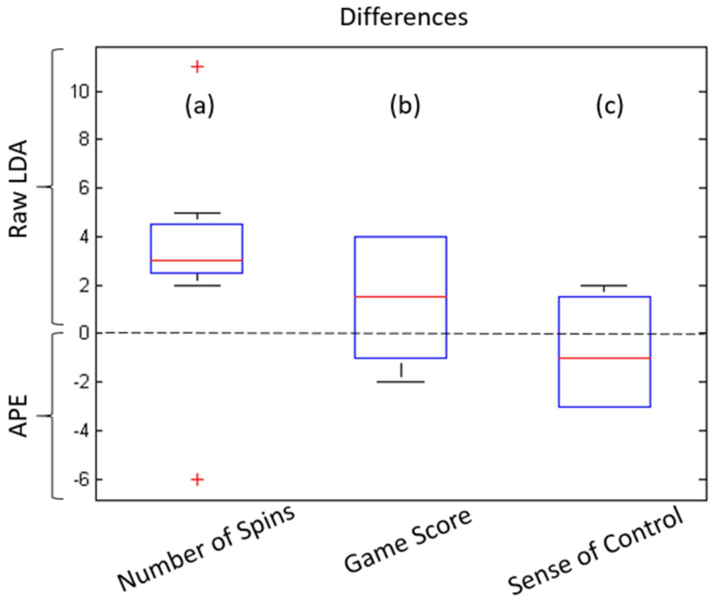

Figure 9.6: In-game data and self-report of control. (a) Number of boat spins (180-degree rotation), (b) game score in terms of flags captured, (c) reported sense of control

When designing APE, we hypothesized that an increased sense of control could provide increased engagement with the task. If a user is more engaged, he/she may try harder and for a longer period. This is important for users who require repeated MI training for rehabilitation purposes. Our assessment of engagement through the engagement index as extracted by the EEG data reveals a non-significant higher engagement during APE (Figure 9.7).

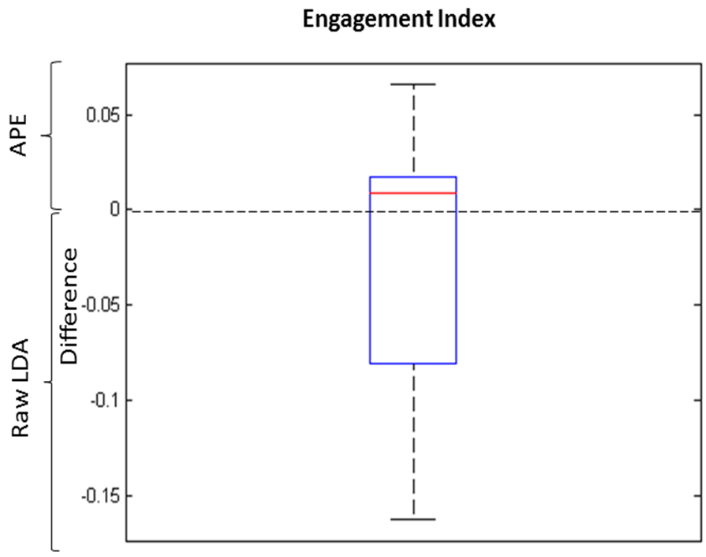

Figure 9.7: Difference in Engagement index as extracted by the EEG bands in equation

Finally, based on the NASA TLX sub-domains (Figure 9.8), users report increased effort and a higher workload index for the APE configuration. Additionally, the reported performance is lower and the levels of frustration are increased. This contrasts with the increased sense of control and engagement during APE.

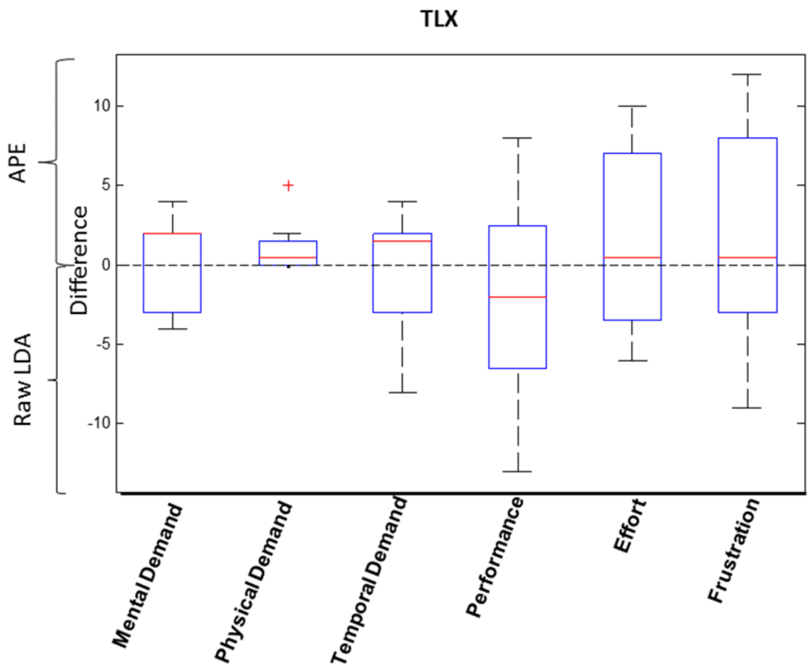

Figure 9.8: NASA TLX sub-domains

9.8 Conclusions

In terms of trajectory and control, when comparing the scores for both conditions, we observe that Raw LDA captures more in-game targets than APE. However, the lower performance for APE could be related to the fact that it is a statistical system that adds a third state to the LDA output, allowing for indecisions during noisy data (Figure 9.6. Instead, the Raw LDA forces the user rowing left or right, making the boat always move towards the flags. Consequently, the added control and confidence on each decision by the APE system -which also translates to fewer decisions being made by the system-leads to more inactivity time, making the user travel less distance, therefore achieving less targets for the same time interval.

Moreover, contrasts with the increased sense of control and engagement during APE may indicate that the increased control that APE affords has as consequence higher mental, physical and temporal demands on users. Hence, making the APE setup a preferred option for users who require continuous training with a MI BCI system.

We show that user control is enhanced through the APE, with a potential increased perceived sense of control and more controlled in-game trajectories. This approach could provide (1) a major assistance for new users and/or neurologically impaired people and (2) increase both perceived and actual performance. To summarize, we showed that NeuRow, combining the use of immersive VR environment, sensory stimulation and adaptive performance, can provide a holistic approach towards MI driven BCIs. In this study, we showcased user performance, user acceptance and important features for self-paced control. Finally, NeuRow's features show promise and potential to be used for MI training in stroke motor rehabilitation.

Chapter 10

Deployment and Clinical Evaluation of APE-driven NeuRow: A Case Study with a Chronic Stroke Patient

10.1 Introduction

Our prior research has shown that MI training in a multimodal BCI setup can provide the strongest motor network activation and similar EEG activation to overt movement-execution [Vourvopoulos and Bermúdez i Badia, 2016]. Moreover, we have showed that combining the use of immersive VR environment, sensory stimulation, and adaptive performance, can provide increased user performance, user acceptance and important features for self-paced control [Vourvopoulos et al., 2016b, Ferreira et al., 2015]. Consequently, NeuRow VR features, as illustrated by our previous findings, show promise and potential to be used for MI training in stroke motor rehabilitation.

Although preliminary success in clinical trials with MI-BCI in stroke rehabilitation has already been shown [Pichiorri et al., 2015], it is difficult to ascertain the efficacy of the underlying principles of MI-BCI systems in a clinical setting because of the lack of long-term evidence to support its clinical relevance [Teo and Chew, 2014]. A major limitation with MI-BCI is a common lack of ability to produce vivid MI and reliable event-related desynchronization (ERD) or event-related synchronization (ERS) of EEG patterns, resulting in poor BCI performance [Allison and Neuper, 2010], and hence recovery. More importantly, after stroke, motor imagery vividness is better when patients are imagining movements on the unaffected than on the affected side[Malouin et al., 2008]. Therefore, it is unclear if previously reported findings will generalize to stroke patients, and what the effect it will have.

In this study we clinically assess NeuRow-VR training paradigm with a chronic stroke patient, undergoing a three-week longitudinal intervention, resulting in 10 BCI-VR training sessions. For this, we included clinical motor assessments and functional brain imaging throughout the intervention, including a follow-up assessment after one month.

10.2 Implementation

10.2.1 Methodology

Clinical Profile

The participant was a 60-year-old male, in the chronic phase of stroke - 8 months post-stroke since the date of the first assessment -, with left hemiplegia resulting from ischemic blockage but without hemispatial neglet. The participant had some vision problems but corrected with eye-wear. He is non-insulin dependent diabetic (diabetes mellitus type 2) and no metal implants (aside from his removable dental prosthesis) were present. He had 4 year of schooling and his experience with computers was reported as very low.

Assessment tools

A set of clinical scales were acquired from the patient in 3 phases. The first before the intervention, serving as baseline, the second after the completion of the intervention and finally a follow-up assessment after one month since the end of the intervention by a trained occupational therapist. The clinical scales included:

- The Montreal Cognitive Assessment (MoCA) assesses several cognitive domains (short-term memory, executive functions, visuospatial abilities, attention, working-memory, language, orientation to time-place), with a score range between 0 and 30 (a score greater of 26 is considered to be normal) [Nasreddine et al., 2005].
- The Modified Ashworth scale (MAS) for measuring spasticity [Ansari et al., 2008]. The score range is between 0 (no increase in muscle tone)

to 4 (affected part rigid in flexion or extension).

- The Fugl-Meyer Assessment (FMA) for motor functioning performance [Fugl-Meyer et al., 1975] with 66 as the maximum score for upper limb.
- The Stroke Impact Scale (SIS), a subjective scale of the perceived stroke impact and recovery as reported by the patient with a maximum score of 100 [Duncan et al., 1999].

In addition, the Vividness of Movement Imagery Questionnaire (VMIQ-2) was used in order to assess the capability of the participant to perform imagined movements from external perspective (EVI), internal perspective imagined movements (IVI) and finally, kinesthetic imagery (KI) [Roberts et al., 2008].

Experimental setup

EEG acquisition: For EEG data acquisition, the Enobio 8 (Neuroelectrics, Barcelona, Spain) system had been used. Enobio, is a wearable, wireless EEG sensor with 8 EEG channels and a triaxial accelerometer, for the recording and visualization of 24 bit EEG data at 500 Hz. The spatial distribution of the electrodes followed the 10-20 system configuration [Klem et al., 1999] with the following electrodes over the somatosensory and motor areas: Frontal-Central (FC5, FC6), Central (C1, C2, C3, C4), and Central-Parietal (CP5, CP6). The EEG system was connected via bluetooth to a dedicated desktop computer, responsible for the EEG signal processing and classification.

HMD: For delivering the visual feedback to the user, the Oculus Rift DK1 HMD was used (Oculus VR, Irvine, California, USA). The HMD is made of one 7” 1280x800 60 Hz LCD display (640x800 resolution per eye), one aspheric acrylic lens per eye, 110^o Field of View (FOV), internal tracking through a gyroscope, accelerometer, and magnetometer, with a tracking frequency of 1000Hz.

Haptic: For delivering vibrotactile feedback, a custom module was used with out-of-the-box components including an Arduino Mega 2560 board and vibrating motors. The vibrating motors (10mm diameter, 2.7mm thick) performed at 11000 RPM at 5V and were mounted inside cylindrical tubes -using 3D printed casing- which act as grasping objects for inducing the illusion of movement during the BCI task. In our setup, a pair of tubes with 12cm of length and 3cm diameter were used.

Virtual Reality feedback: The BCI-VR task involved the use of NeuRow VR together with APE as described in Chapter 6 and 7 (Figure 10.1).

Figure 10.1: System setup, including the wireless EEG system, the HMD, together with headphones reproducing the ambient sound from the virtual environment. Patient holds the vibrotactiles modules supported by a custom-made table-tray, similar to the wheelchair trays used for support.

BCI Protocol and Data Analysis

Protocol: The first step of the training consisted on the acquisition of the raw EEG data to train a linear classifier to distinguish between Right and Left imagined hand movements. Throughout the training session, the user performs mental imagery of the corresponding hand (based on the presented stimuli). For each hand, the user is stimulated visually (VR action observation), auditorily, and haptically through the vibration on the corresponding hand. The training session was configured to acquire data in 24 blocks (epochs) per class (Right or Left hand imagery) in a randomized order. Following the training, data are used to compute a Common Spatial Patterns (CSP) filter, a spatial filter that maximizes the difference between the signals of the two classes for increased performance, thus, has become a standard tool in the use of MI-based BCIs [Lotte, 2014]. Finally, the raw EEG and the spatial filter are used to train a Linear Discriminant Analysis (LDA) classifier. LDA has very low computational requirements, is simple, making it ideal at generalizing to unseen data, hence, the most used classifier for BCI design [Lotte, 2014].

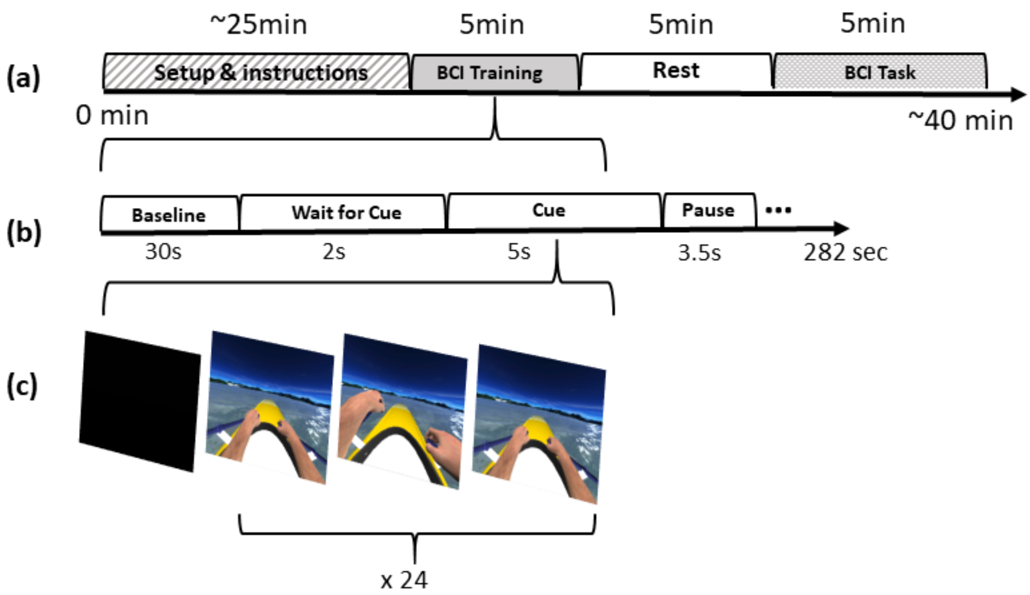

Figure 10.2: BCI Protocol. (a) Intervention stages including the setup, training, resting period and finally the BCI task. (b) The training stages. (c) Training feedback distributed in 24 epochs per class [left—right]

Data analysis: EEG signals were processed in MATLAB (MathWorks Inc., Massachusetts, US) with the EEGLAB toolbox [Delorme and Makeig, 2004] for filtering, artifact rejection, epoching, and computing the absolute power (uV^2/Hz). The power spectrum was extracted for the following frequency bands: Delta (1 - 4 Hz), Alpha (8 - 13 Hz), Beta (13 - 30 Hz), Theta (4 - 8 Hz), and Gamma (30 - 80 Hz). In addition, the Engagement Index

(EI) was computed from the EEG bands, for comparison with prior studies as described in previous chapters. Finally, Independent Component Analysis (ICA) was used for removing major artifacts related with power-line noise, eye blinking, ECG and EMG activity.

fMRI Protocol and Data Analysis

Protocol: Functional magnetic resonance imaging (fMRI) data were acquired on a 3T GE Signa HDxt MRI scanner (General Electrics Healthcare, Little Chalfont, United Kingdom) using the standard 12-channel head matrix coil.

During functional measurements the imaging volumes ($3.5 * 3.5 * 3.5$ mm voxels, 0.75 mm gap, TR = 2.5 s, TE = 30 ms, FoV = $224 * 224\ mm^2$, flip angle=90^o, 36 transversal slices) were obtained within one block (stimulus block = 20 sec, control block = 20 sec, total duration = 5.33 min)). During scan, the patient underwent three conditions. (a) First was instructed to execute a sequential finger-tapping task (index-middle-ring-little-index-middle-ring-little) from a first-person perspective with his non-affected arm. (b) Secondly, the patient had to imagine the kinesthetic experience of the same task (finger-tapping) for both the right and left hand based on the provided stimulus/instruction. Each trial starts with a fixation cross, followed by a red arrow pointing to the right or left (presented for 20 s), indicating the beginning of a movement execution/imagination period, known as the standard Graz Motor Imagery protocol [Pfurtscheller et al., 2003]. (c) Finally, the patient had to imagine the kinesthetic experience of the rowing task from NeuRow VR [Vourvopoulos et al., 2016b] from the first-person perspective for both the right and left hand based on the provided stimulus [see Figure 10.3]. Each trial starts with the boat floating without rowing, as baseline,

-substituting the fixation cross of the previous condition-, then for each hand, the corresponding movement was initiated for left or right rowing.

The visual feedback was delivered -synchronized with the console computer- through specialized MR compatible fiber-optic goggles at a resolution of $640{*}480$ pixels.

After the experimental task a high-resolution structural volume was also obtained using a T1-weighted magnetization-prepared rapid-acquisition gradient echo (MPRAGE) sequence (TR = 6.552 ms, TE = 2.82 ms, FoV = $256 * 256\ mm^2$, flip angle = 14^o, slice thickness = 1 mm, transversal slices) followed by Diffusion Tensor Imaging (DTI) sequence (TR = 10000ms, TE = 86 ms, FoV = $256 * 256\ mm^2$, flip angle = 90^o, slice thickness= 4.7 mm, transversal slices).

Data Analysis: Standard pre-processing steps were applied to functional data through FSL [Smith et al., 2004] prior to further analyses, including: 1) the first three volumes were discarded to allow for the net magnetization to reach a steady-state; 2) removal of non-brain tissues using the FSL's tool BET; 3) estimation and correction of head movements using the FSL's tool MCFLIRT; 4) high-pass temporal filtering with a cut-off period of 100 s; and 5) Gaussian spatial smoothing with a full width at half-maximum (FWHM) of 5 mm.

A model of the BOLD signal was built based on a boxcar function, taking the value of 1 during the periods of task, and 0 during the periods of rest. This model was convolved with a standard double-gamma hemodynamic response function (HRF), and fitted to the pre-processed fMRI data using the FSL's tool FILM, which uses a general linear model (GLM) framework. Voxels exhibiting BOLD changes significantly correlated with the model were subsequently identified by cluster thresholding (voxel $Z > 2.3$, cluster $p < 0.05$). This procedure was done for each condition separately.

In order to quantify the impact of the different conditions on motor activation, the BOLD activation maps obtained for each condition were then masked using motor and somatosensory functional masks (for the left and right hemispheres) obtained from the Juelich Histological Atlas [Eickhoff et al., 2005]. These are probabilistic maps and were thresholded at 40%. The average Z-score across voxels belonging to each mask was computed, and used as a measure of motor activation.

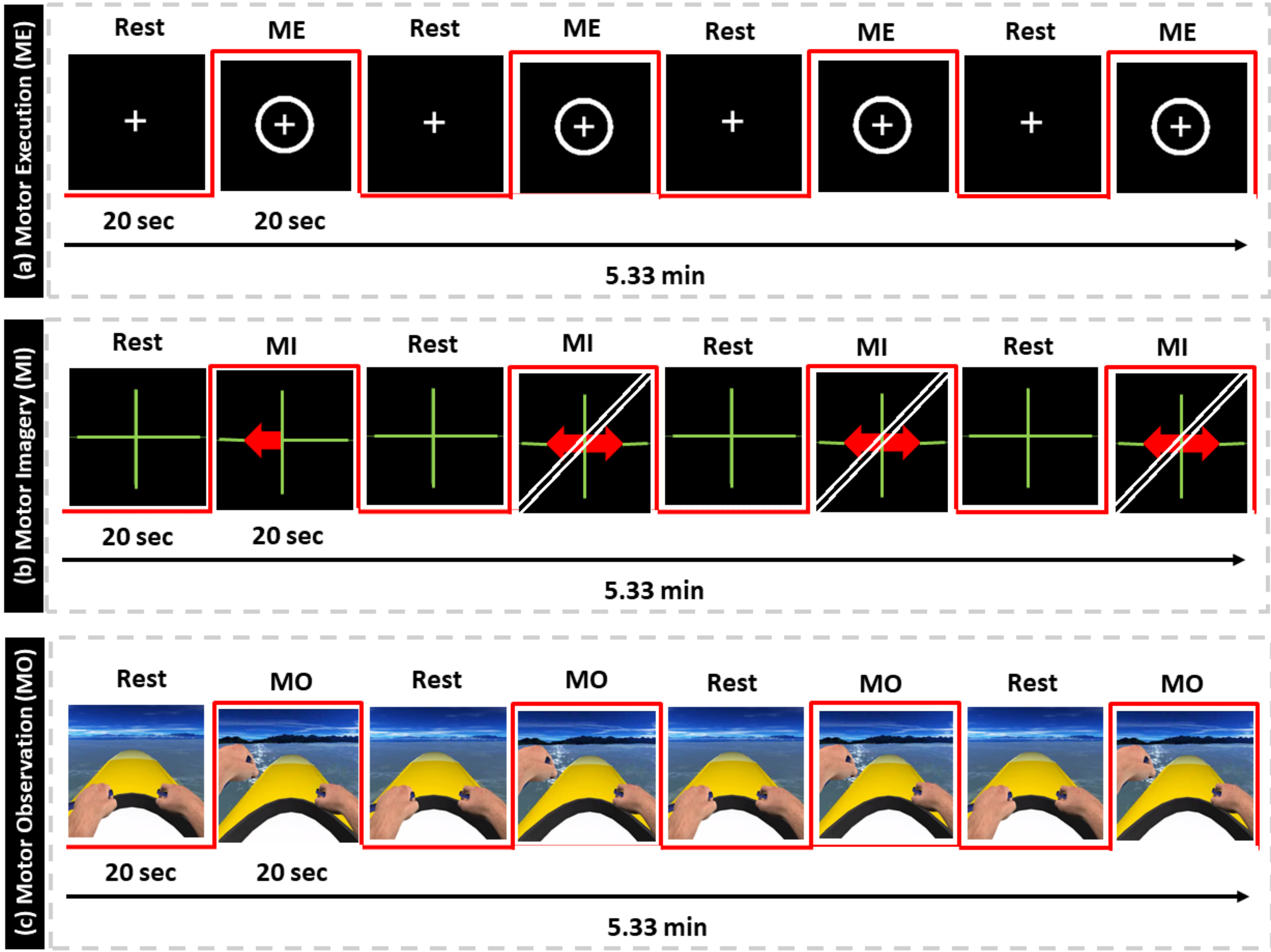

Figure 10.3: fMRI protocol. (a) Motor-Execution feedback, (b) Motor-Imagery feedback with directional arrows, (c) Motor-Observation feedback of NeuRow

10.2.2 Results

The patient undergone 3 weeks intervention with NeuRow, in a clinical environment, resulting in 10 BCI sessions using VR. Clinical scales, motor-imagery capability assessment, and functional -together with structural- MRI data had been gathered in three periods. Finally, electroencephalographic (EEG) data had been gathered during all sessions, resulting to more than 20 datasets of electrical activity.

Moreover, the participant provided his written informed consent before participating in the study. This study was conducted with the collaboration of the Hospital "Dr. Nélio Mendonça" in Funchal (protocol no. 15/2015) [Appendix C], and the local healthcare system of Madeira region (SESARAM - Serviço de Saúde da RAM, E.P.E.).

Clinical Improvements:

In terms of motor functioning as assessed by the FMA scale, the patient showed an improvement of 9 points after the end of the intervention, (Pre: 31, Post: 40), followed by an improvement of 4 points (follow-up: 44) after one month (see Table 10.1). Concerning spasticity levels, MAS score showed slight increase in muscle tone (Pre: 1+, Post: 2) but returned to 1+ as recorded in the follow-up assessment.

On the cognitive domain, no differences were observed during pre-post and follow-up assessments.

Through the self-reported impact of stroke as given by the SIS, patient reported a big increase in "strength" followed by a small increase in "ADLs" and the "physical domain" (see Table 10.2). For "hand Function", "Emotion" and "Handicap", the patient reported a small decrease, remaining stable at the follow-up. Finally, the reported "Mobility", "Memory", "Communica-

Table 10.1: Clinical Scales

	FMA	MoCA	MAS
PRE	31	20	1+
POST	40	21	2
FOLLOW-UP	44	18	1+

Table 10.2: SIS Scales

	Strength	Hand Fucntion	Mobility	Memory	ADL & IADL	Commu-nication	Emotion	Handicap	Physical Domain	Stroke Recovery
PRE	50	100	100	100	95	100	97.2	100	86.3	70
POST	87.5	95	100	100	97.5	100	94.4	87.5	95	70
FOLLOW-UP	87.5	95	100	100	97.5	100	94.4	87.5	95	70

tion" and "Stroke Recovery" remained stable across pre-post and follow up, having the highest score.

Overall, motor function has improved considerably, maintaining also a high level following intervention (FMA pre: 31, post: 40, follow-up: 44). In contrast, MoCA and MAS changes are very small. FMA improvement is reflected by the perceived strength and physical domain capability through SIS.

Comparison with other VR interventions

For illustrating the differences in recovery compared to stroke population that undergone virtual rehabilitation or virtual-reality based rehabilitation, a dataset from a prior longitudinal study of similar length and intensity had been used for comparison [Faria et al., 2016]. The comparison dataset includes clinical scales from 8 stroke survivors that underwent a combined

VR treatment for 4 weeks, (both in motor and cognitive domains) using an upgraded version of the TPT-VR game [Vourvopoulos et al., 2014a], the Reh@task.

As illustrated in Figure 10.4, the FMA score of 31 from the baseline measurement of the patient is close to the Median score of the VR intervention group (Mdn = 30.5, SD = 16.4), but post assessment and follow-up score shows much higher improvement compared to the group data. Concerning MoCA, the patient cognitive ability is much lower than the average of the VR group (Mdn = 26, SD = 2.6), there is an improvement in the post-assessment but drops again in the follow-up. This difference between the patient and the VR group is greater, showing the effect of cognitive training which the VR group had during its intervention. In terms of spasticity, the patient shows an initial improvement in MAS score but drops back to the same level but within the range of the VR group after treatment (Mdn = 1.75, SD = 0.74).

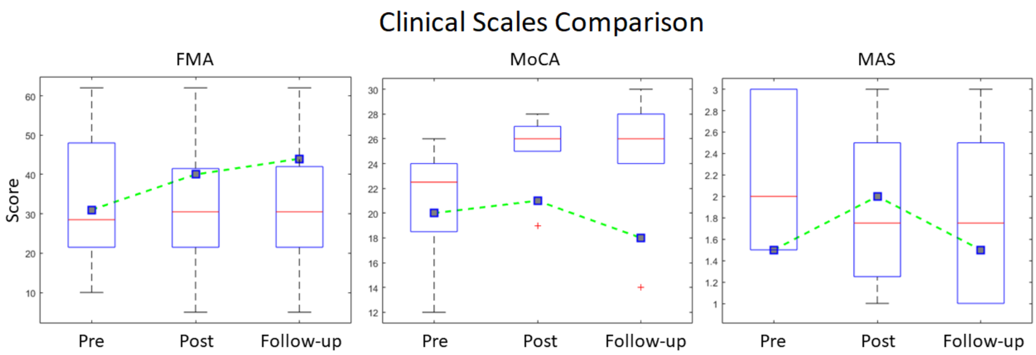

Figure 10.4: Distributions of clinical score of 8 patients from a combined motor/cognitive VR intervention [Faria et al., 2016] compared with case study patient score (data points) using only MI-BCI training in VR (pre, post, follow-up).

Motor-Imagery Capability

VMIQ pre-post-follow: Patients capability for vivid motor-imagery, was assessed through 3 sub-scales of VMIQ-2, external visual imagery (EVI), internal visual imagery (IVI) and finally kinesthetic imagery (KI). All three sub-scales were assessed pre-post the intervention together with a follow-up after one month. Pre-assessment showed a low level in external imagery capability (EVI = 19) compared to internal imagery (IVI = 47) and kinesthetic imagery (KI = 43). Post-assessment showed a notable increase in external imagery capability (EVI = 47) and a more stable score for internal (IVI = 48) and kinesthetic (KI = 44). Finally, in the follow-up assessment, the score stabilized for all sub-scales (EVI = 47, IVI = 47, KI = 39) [see Figure 10.5].

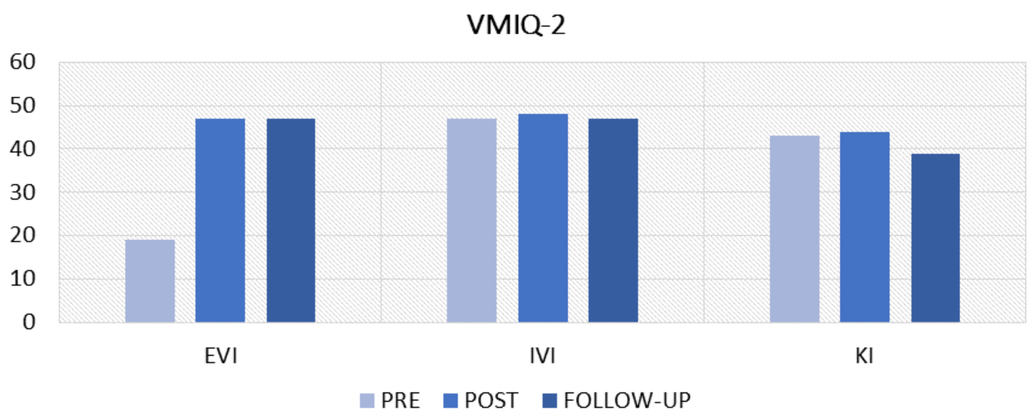

Figure 10.5: VMIQ-2 sub-scales for external visual imagery (EVI), internal visual imagery (IVI) and kinesthetic imagery (KI)

Comparison with healthy: Comparing the motor-imagery capability data of the VMIQ-2 questionnaire, with a group of healthy participants (N=8) that undergone the same BCI protocol from a previous study [Vourvopoulos et al., 2016b], we can estimate a "normal" range for motor-imagery capability of healthy population as a reference. Concerning the difference in EVI comparing pre-post assessments of our patient, we can see a big leap after the BCI-VR intervention, overpassing even the average score of the healthy group (see Figure 10.6). Comparing the IVI and KI scores that showed stable or no change, we can see that are within the healthy range of the reported motor-imagery capability.

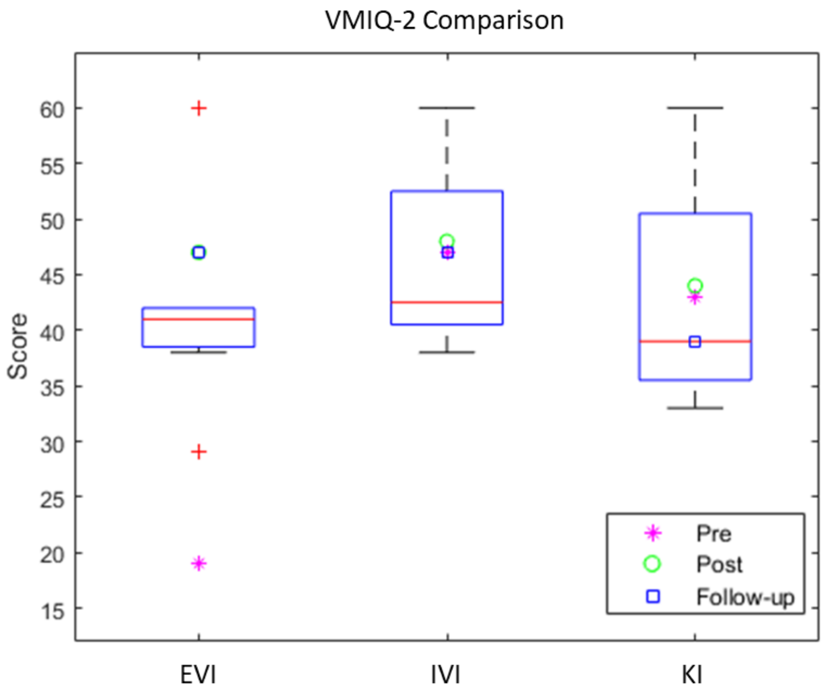

Figure 10.6: VMIQ-2 comparison with healthy data

BCI Performance

Classifier Performance: The overall classification performance during training across 10 sessions, it stayed stable around 60% (see Figure 10.7).

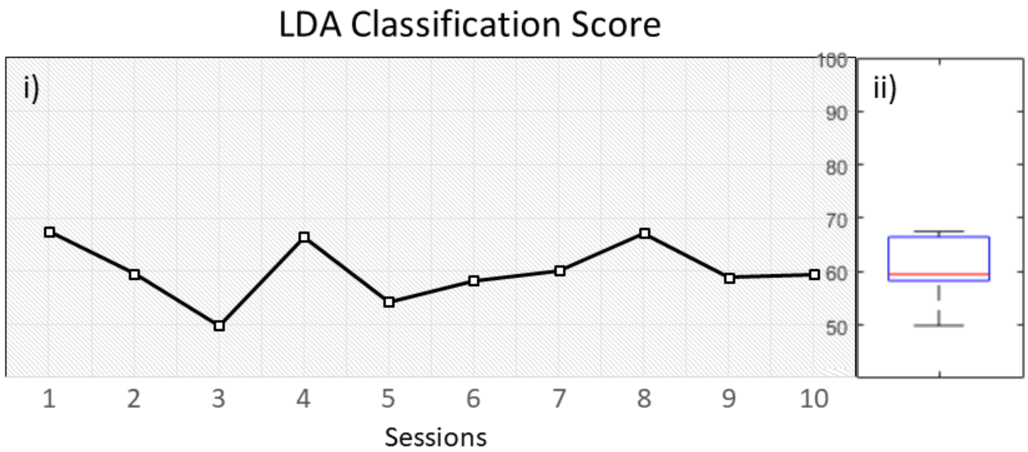

Figure 10.7: LDA classification performance over time within 10 sessions

Comparing the training data from the first and last session, we used the trained classifier performance to assess how well it can differentiate between the two classes (left—right). We extracted the results in terms of probability classification of right vs left. For a total of 48 events (24 epochs per class), and since the classes are balanced, a perfect classifier output should have an average probability 0.5 per class/hand. Looking at the differences between the first (pre) and the last session (post), in figure 10.8 is illustrated an initial imbalance between the Left (Mdn = 0.42) and the Right hand (Mdn = 0.58), but this difference is reduced after the MI-BCI intervention, with the Left hand (Mdn = 0.52) being closer to the Right (Mdn = 0.48).

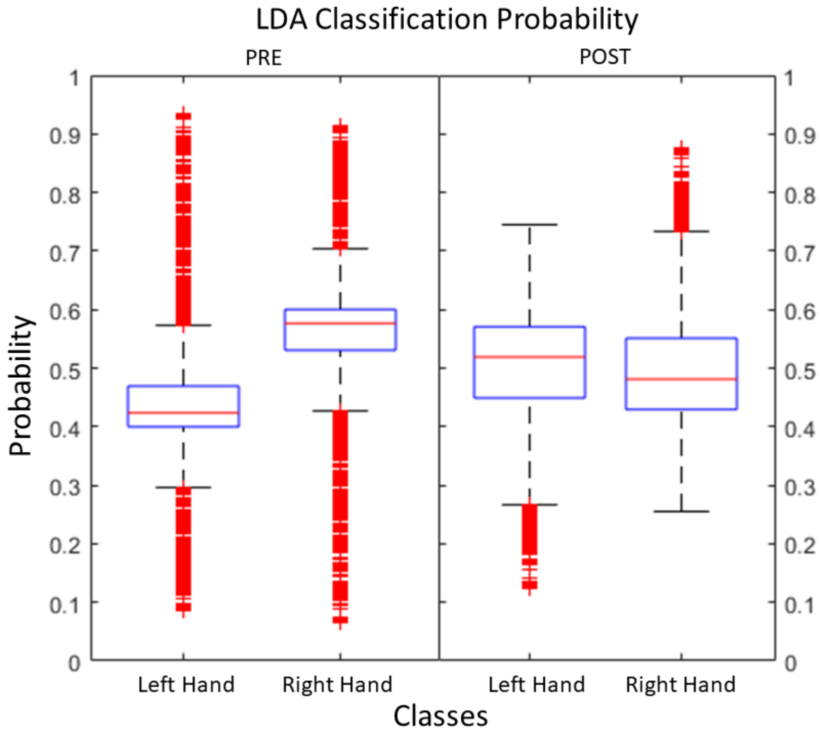

Figure 10.8: LDA classification probability

LDA Comparison: The classification score across all sessions was compared with two groups of healthy users. First with a group of participants (N=8) that undergone the same BCI protocol from a previous study [Vourvopoulos et al., 2016b] [VR group] and secondly with a group of studies (N=11)[Vourvopoulos et al., 2016a] that used the same feature extraction method (band power with CSP) and classifier (LDA) for two-classes (left/right hand) MI data [non-VR Group]. Results show that NeuRow setup with healthy participants (Mdn = 76), precede both the non-VR group (Mdn = 65) - as reported in a previous study [Vourvopoulos et al., 2016b] - and the patient classification score across all sessions (Mdn = 60) (see Figure 10.9). Using the VR group with NeuRow as a reference point - since the same setup as on the intervention was used - we can see that a non-healthy user in a VR setup is closer to the performance of the non-VR group, showing a strong effect of the VR component in performance. Overall, non-healthy VR closer to healthy non-VR.

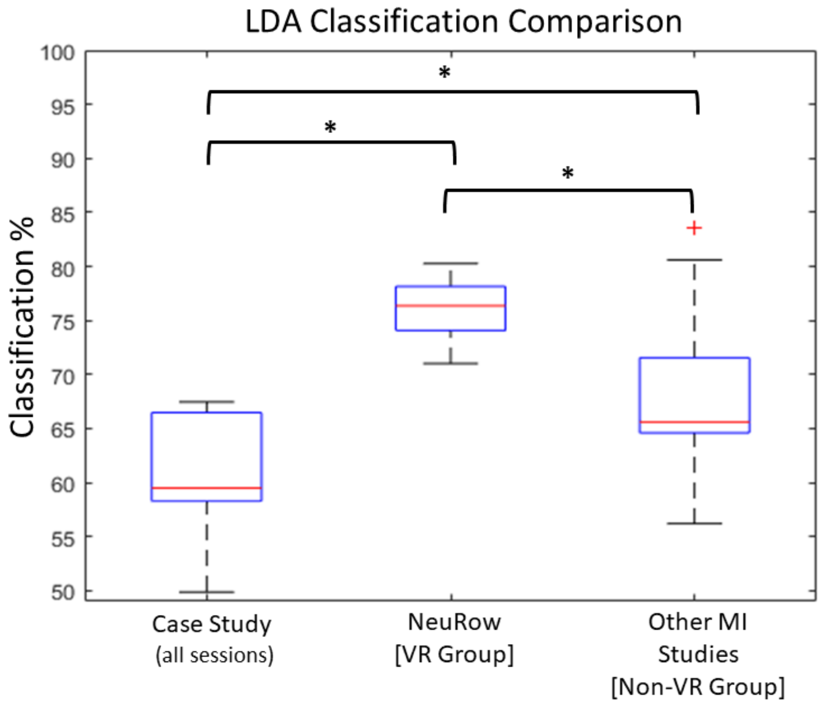

Figure 10.9: LDA Comparison with healthy. Statistically significant differences between Case-study, VR and non-VR groups has been observed (p <0.05)

Finally, while current classification score shows an effect from VR component, there was a statistically significant difference between groups as determined by one-way ANOVA ($F(2,27) = 15.09$, p ¡ .001). A Tukey post-hoc test revealed that the patient LDA score was statistically significantly lower compared both VR Group (NeuRow) and non-VR Group.

EEG Bands Activation

EEG bands: Previous findings have showed that increased capacity to modulate brain activity patterns in all extracted EEG bands during MI, are matching more closely those present during motor-execution [Vourvopoulos and Bermúdez i Badia, 2016]. Extracting the absolute Power from the EEG bands and comparing the first (pre) with the last (post) session, we can see an increase in power across all bands (see Figure 10.10).

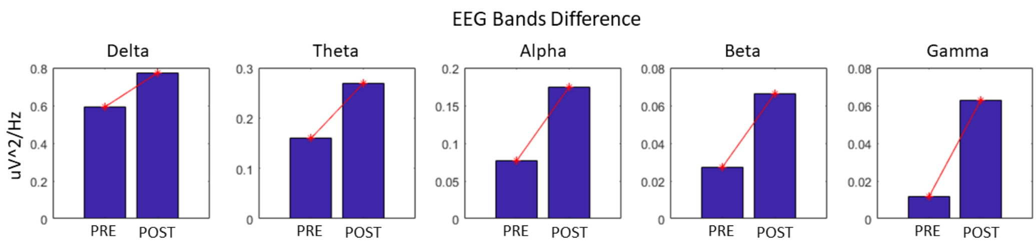

Figure 10.10: EEG bands pre-post

Finally, from the extracted event-related potential (ERP) averages of left and right EEG trials, we can identify a clear contralateral activation in band Power after the BCI-VR intervention (see Figure 10.11).

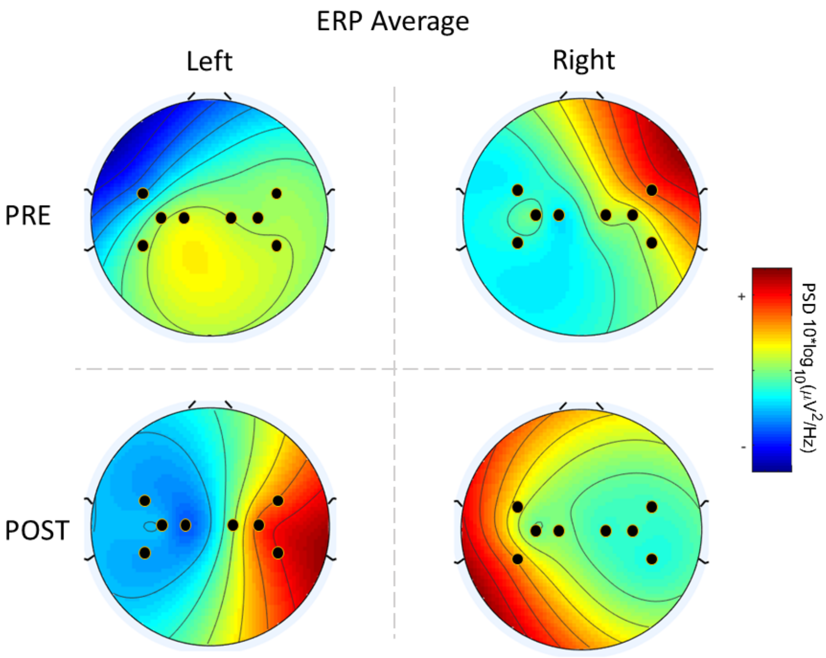

Figure 10.11: Event related potentials pre-post per class

Comparison with healthy: Comparing the evoked EEG activity during training with data from healthy participants -which used the same experimental setup [Vourvopoulos et al., 2016b]-, we can observe a consistent trend between the first and last session (see Figure 10.12). EEG power from healthy participants which used the same experimental apparatus, can serve as a reference point on where "normal" EEG modulation boundaries are. For all EEG bands, we found that the EEG power on the first session (pre) is in the lower quartile (Q1) of the distribution while on the last session the EEG power is always higher and closer to the Median of the healthy distribution inside the Interquartile Range (IQR). Current results, clearly indicate a convergence towards the healthy group EEG power.

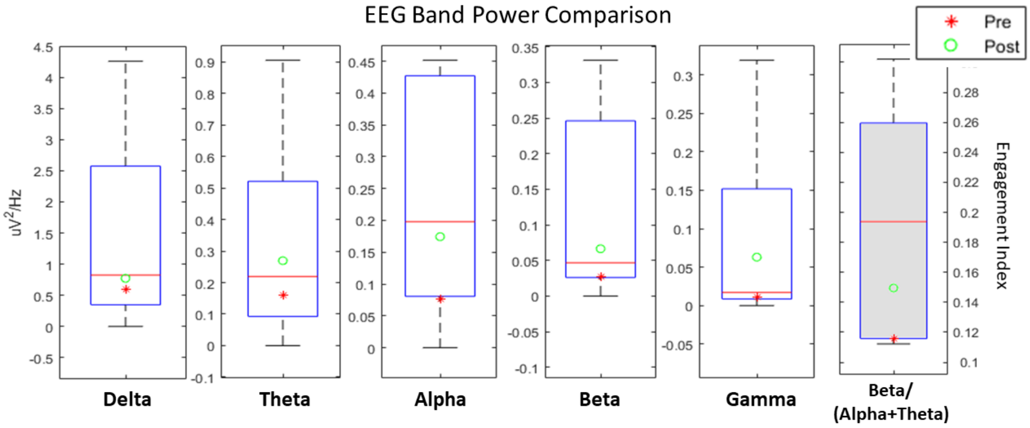

Figure 10.12: EEG Comparison with healthy users

Functional Magnetic Resonance Imaging

In this section we present an analysis of functional magnetic resonance imaging (fMRI), comparing brain activity between motor-execution of the healthy arm (ME), motor-imagery (MI) and motor-observation (MO) of the NeuRow VR feedback. Scans have been performed pre and post the BCI-VR intervention including also a follow-up scan a month after.

Analyzing the brain imaging data from all three conditions, during pre-post and follow-up of the intervention, we generated a set of brain maps in terms of z score (see Figure 10.14). z is a statistical parameter, making fMRI analysis a form of statistical parametric mapping. Higher z scores mean more likely activation. Moreover, by using an anatomical atlas mask [Eickhoff et al., 2005] from the motor cortices (MC) and the somatosensory cortices (SSC), we calculated brain activation in terms of average z score over the MC and SSC areas.

Differences before and after the intervention. The motor-execution (ME) task, which involved the finger tapping from the healthy right arm, evoked increased activation in both contralateral MC and SSC, between pre (z = 3.7) and post (z = 5.49) scans (see Table 10.4). Average activation drops back almost to the same level on the follow-up scan (z = 3.64).

During paretic hand motor-imagery (MI), the activation on the contralateral non-paretic MC increased steadily between pre scan (z = 3.28), post scan (z = 3.78) and follow-up (z = 4.1). The same monotonous trend was observed as well over the non-paretic SSC with increased average z score between pre scan (z = 3.16), post scan (z = 3.87) and follow-up (z = 3.99) (see Table 10.4).

For right hand motor-imagery (MI), the activation on the contralateral left MC increased also between pre scan (z = 2.7) and post scan (z = 3.23) but reduced back in the same levels on the follow-up (z = 2.73). Similar trend was observed as well over the left SSC with increased activation between pre scan (z = 2.74) and post scan (z = 3.56) but reduced in follow-up (z = 3.06)(see Table 10.4).

Overall, we can identify a trend in increased activation during paretic hand MI in both over MC and SSC between pre-post and follow-up scan. For non-paretic hand MI there is an increased activation between pre-post scans -in the contralateral hemipshere- but it drops back to the initial (pre-intervention) activation in the follow-up over both MC and SSC. Moreover, contrallateral activation was higher in both MC and SSC during paretic hand MI than during non-paretic hand MI. This difference between paretic—non-paretic MI is increased between pre, post and follow-up (see Table 10.3).

On left hand motor-observation (MO), of rowing through the NeuRow VR feedback, the activation on the contralateral right MC increased steadily between pre scan (z = 3.26) and post scan (z = 4.18) but dropped on follow-up (z = 2.64). On the right SSC, average z score is increased between pre

Table 10.3: z score differences between paretic—non-paretic motor-imagery(MI) and motor-observation (MO) for pre-post and follow-up scan

	MI		MO	
	MC	SSC	MC	SSC
PRE	0.58	0.42	3.26	3.07
POST	0.55	0.31	1.25	0.16
FOLLOW-UP	1.37	0.93	0.39	3.28

scan (z = 3.07) and post scan (z = 3.65) but no activation was observed on follow-up (z = 0)(see Table 10.4).

For right hand motor-observation (MI) of rowing, the activation on the contralateral left MC increased between pre scan (z = 0), post scan (z = 2.93), keeping almost the same level on the follow-up (z = 3.03). Over the left SSC, on the pre scan there was no activation as-well (z = 0) but increased in post scan (z = 3.81) maintained in follow-up (z = 3.28)(see Table 10.4).

Comparing left hand MO with right hand MO, we see activation only for the left hand in the pre-intervention scan over both MC and SSC (see Table 10.4. On the post scan, activation in both cortices rises for both hands with a higher activation on the left hand MO. On the follow-up, the balance changes towards the right hand with higher activation compared with post scan but also the left hand (see Table 10.3).

Differences Between Conditions. By comparing activation between conditions, we see that on pre-intervention scan over left MC and SSC, the highest activation is during ME and no activation during MO. In post scan, again ME is the highest, followed by MI and lastly by MO. On the follow-up scan, we observe that MO has very similar activation with ME, surpassing MI in both MC and SSC.

In right MC and SSC, we observe that pre scan MI activation is similar to MO activation. The same trend is observed also in the post scan but dropping in the follow-up scan for MO activation only in right MC but not in SSC (see Figure 10.13).

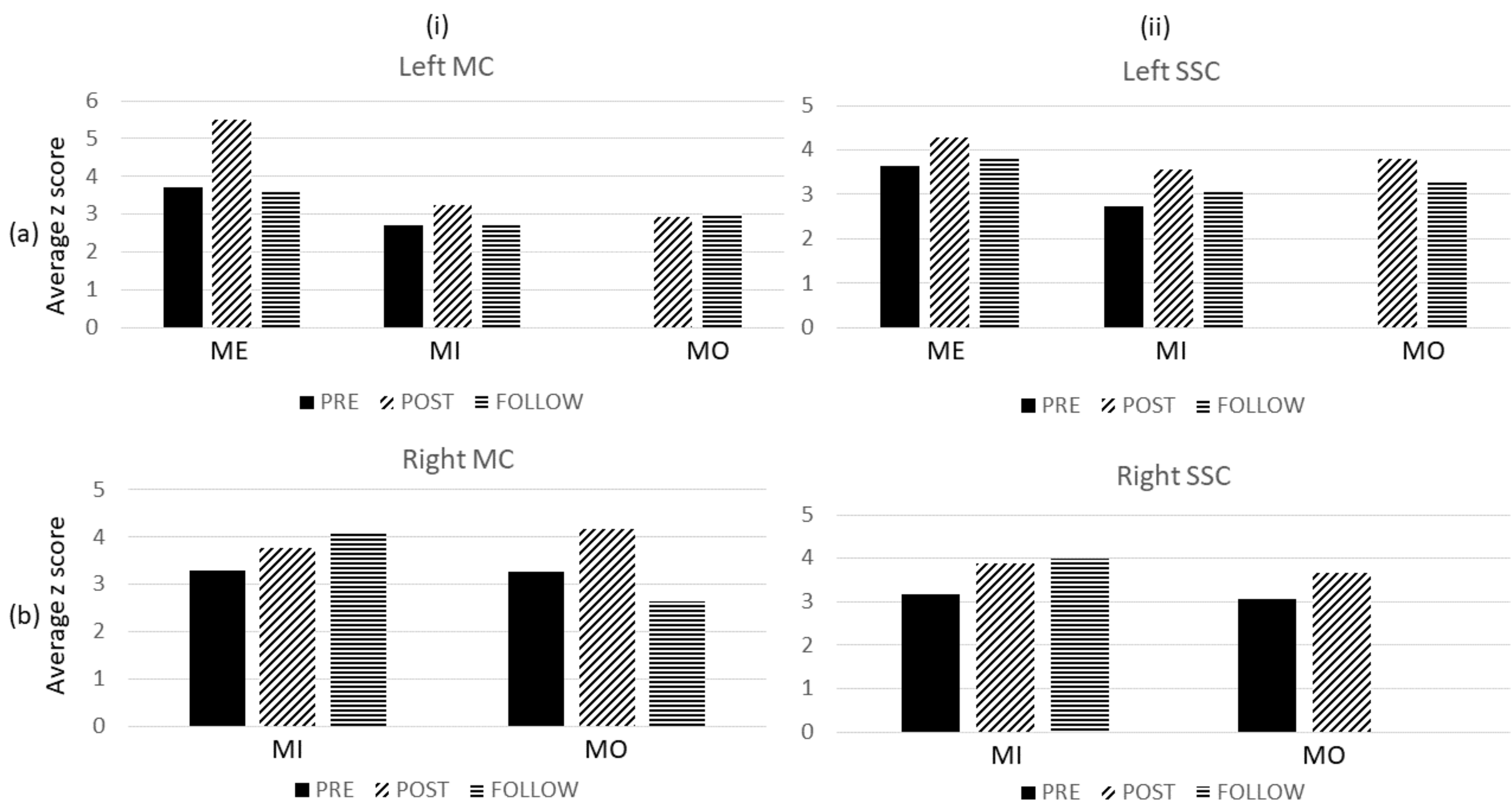

Figure 10.13: Average activation z score. Horizontal: (a) Left and (b) right hemipsheres. Verical: (i) motor cortex (MC) and (ii) somatosensory cortex (SSC)

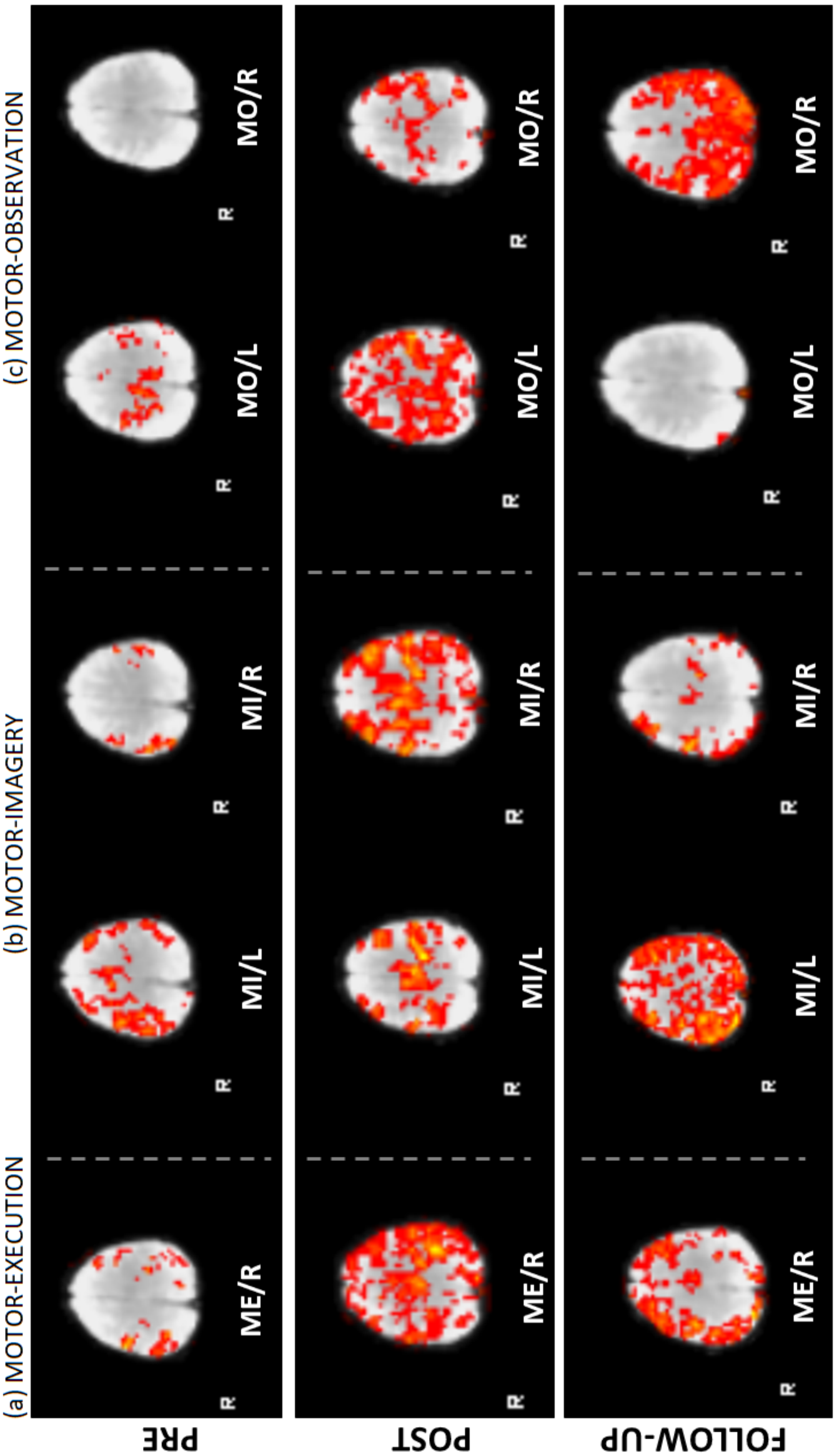

Figure 10.14: Brain maps. MC and SSC activation between scans

Table 10.4: Average z score extracted from left—right hemisphere from the motor cortex (MC) and the somatosensory cortex (SSC). The score involve the right hand motor-execution (ME), motor-imagery (MI), and motor observation (MO) from both hands. Grayed cells indicate contralateral activation

Mask	Scan	ME RIGHT	MI LEFT	MI RIGHT	MO LEFT	MO RIGHT
	PRE	3.7	2.72	2.7	2.95	0
MC Left	POST	5.49	2.85	3.23	3.56	2.93
	FOLLOW	3.64	3.21	2.73	2.5	3.03
	PRE	3.19	3.28	3.22	3.26	0
MC Right	POST	3.17	3.78	3.24	4.18	3.27
	FOLLOW	3.25	4.1	2.73	2.64	2.84
	PRE	3.63	2.96	2.74	2.72	0
SSC Left	POST	4.28	3.47	3.56	3.77	3.81
	FOLLOW	3.85	3.19	3.06	0	3.28
	PRE	3.37	3.16	3.18	3.07	0
SSC Right	POST	3.4	3.87	3.77	3.65	0
	FOLLOW	3.69	3.99	2.74	0	2.97

10.2.3 Conclusions

Initial results show clear improvements and recovery regarding motor function in terms of clinical scales, self-reported scales, electrophysiological data and finally brain imaging data.

In terms of clinical scales, FMA has shown a stable increase in motor functioning followed throughout all assessments. This shows a carryover effect. Prior studies have shown that for carryover effect to take place, carryover-mechanisms of action are based on movement prediction and sense of agency/body ownership. Moreover, the carryover effect influences the ability of a patient to plan the movement and to perceive the stimulation as a part of his/her own control loop [Gandolla et al., 2016]. That could indicate effective motor learning partially evoked by immersive VR through NeuRow.

We, therefore, hypothesize that a multimodal, immersive VR BCI training could have enhanced the carryover effect of the rehabilitation process that could eventually be reflected in terms of increased ADLs.

Regarding the levels of spasticity, MAS has shown only an increase during the intervention time as given by the pre-post assesments but falling back to the previous level in the follow-up assessment. Finally, cognitive scores are low, showing mild cognitive impairment values, with prior studies defining 26 as the cut-off level for dementia [Davis et al., 2015].

Comparisons of current clinical scales results with a stroke group that undergone a combined motor/cognitive VR rehabilitation treatment [Faria et al., 2016], showed larger improvements in FMA with the BCI-VR intervention.

In terms of the perceived impact of stroke through the SIS questionnaire, strength (pre: 50, post: 87.5, follow-up: 87.5), ADL (pre: 95, post: 97.5, follow-up: 97.5), and physical domain (pre: 86.3, post: 95, follow-up: 95) levels have been improved.

Increased motor-imagery ability, as reported by VMIQ-2, but also as captured by the EEG data through the Alpha and Beta bands, seem to manifest motor recovery. Hence our methodology for, motor-imagery training may provide a valuable tool to access the motor network and improve outcome after stroke. This is in line with prior research findings illustrating better functional outcome in the BCI group, including a significantly higher probability of achieving a clinically relevant increase in the FMA score [Pichiorri et al., 2015]. Additionally, the comparison with healthy data, reveals a convergence towards "normal" motor-imagery ability in all domains (external, interval and kinesthetic), and also maintaining a high score in follow-up.

Comparing the EEG band Power activation, pre-post, we can clearly observe big improvements. This was also observed in a prior study where enhanced activation of brain patterns was identified during motor-execution [Vourvopoulos and Bermúdez i Badia, 2016]. Moreover, using as a point of reference healthy data -undergoing the same BCI training-, we can see that post intervention, EEG data are closer to the distribution of the healthy. Since motor-imagery involves to a large extent the same cortical areas that are activated during actual motor preparation and execution [Jeannerod and Frak, 1999], this increase is likely to be indicative of motor recovery.

Overall BCI performance in terms of classification score through the LDA was stable throughout all sessions. Nevertheless, EEG brain maps and classification data show convergence towards healthy population activation.In addition, compared with two healthy groups (VR and non-VR), we can see again that VR can result into better classification score compared with standard training [Vourvopoulos et al., 2016b, Vourvopoulos and Bermúdez i Badia, 2016], although with the patient showing better performance. This can highlight once more the importance of the VR feedback and the role of agency in BCI performance.

Finally, the analysis of the brain imaging data, showed an increased activation -in terms of average z score- in both the motor and somatosensory cortices for motor execution of the finger-tapping task and motor imagery. Concerning motor observation of the rowing task, activation over the motor and somatosensory cortices is only apparent after the BCI intervention in the post and follow-up scans. This finding support the hypothesis that BCI-VR training can promote the reorganization of brain networks related not only to action execution but also in observation. This would be consistent with the recruitment of the MNS during training.

Therefore, a tailored BCI-VR training paradigm could help preventing maladaptive plasticity -avoiding compensatory movements- rather helping to develop normal movement patterns.

Summarizing, through this case study, we have been able to test our proposed BCI-VR paradigm, acquiring information from various sources. Clinical scales illustrated large improvements in motor function, electrophysiological data showed an increase in brain activation -similar to healthy subjects- and brain imaging data have showed the effect of motor-imagery training and VR feedback, promoting plastic changes in the targeted areas of the brain. Our findings extend prior research that showed the efficacy of BCIs using MI for motor rehabilitation [Pichiorri et al., 2015, Silvoni et al., 2011]. However, the majority of previous studies have not addressed the effect of agency and embodiment through VR feedback. These results suggest that this approach can be used with patients in the chronic stage who showed no improvement during conventional therapy. As this is a case study, additional research is needed to explore this hypothesis including combined brain data with electrophysiological information during training. This will allow us to optimize motor learning, identify "good" plasticity and finally identify the specific benefits of brain-controlled VR training environments in neurorehabilitation.

Neurofeedback Summary

For the inclusion of patients which cannot benefit form current virtual rehabilitation tools due to low mobibility, The RehabNet framework was extended with the development of neurofeedback tools through the utilization of Brain-Computer Interfaces. By identifying limitations in current brain-to-VR interaction, especially for people after stroke, we performed a set of studies for optimizing brain-computer interaction. In terms of cost and accessibility, different EEG systems had been assessed for their cost-effectiveness, broadening the accessibility of the RehabNet framework. Next, by investigating the role of motor-priming in a BCI-VR paradigm as-well-as the user profile and prior gaming experience, we have been able to identify ways to maximize BCI performance of first-time users. Building on top of these findings, NeuRow, a multimodal BCI-VR environment for MI training was developed together with a pilot assessment for adaptive performance. This resulted to the test-bed of our proposed Neurofeedback paradigm. This system has been tested with a stroke patient in a longitudinal clinical study combined with functional brain imaging. Through this case study, we have been able to show in terms of motor function, increased brain activation through electrophysiological data and through brain imaging data.

Part IV

Conclusions and Discussion

General Conclusions

The RehabNet framework is an integrative platform for neuroscientists, engineers and clinicians to further study stroke recovery and improve the impact of rehabilitation strategies.

This research brought further insights on how to improve the effectiveness of ICT tools and methodologies for rehabilitation after stroke. Through a set of studies, multiple contributions have been provided in this area.

From the technological point of view, the design of RehabNet framework is focusing on integrative motor and cognitive therapy based on VR scenarios that address both domains in re-training stroke patient abilities. Thus, with current technology, we provide a more ecologically valid rehabilitation toolbox that can be utilized in virtual rehabilitation scenarios and consequently, to have a greater impact in the activities of daily living of the patient in terms of independence and improvement of performance. Further, through different interaction interfaces, the RehabNet framework tools are accessible to a wide range of patients.

During the project, novel rehabilitation scenarios had been developed including: a cognitive-motor training cancelation task in VR, a simulated city for the training of Activities of Daily Living in an ecologically valid context, and a Motor-Imagery based BCI system that combines VR with EEG based neurofeedback for motor rehabilitation.

This project has broadened modern VR rehabilitation approaches to (1) include those patients with worse prognostic (motor and cognitive) through an accessible and interface-independent architecture; (2) provide very low-cost at-home rehabilitation solutions by making available all developed technology for free to the community; and (3) we have brought new insights on the impact and use of VR technologies for rehabilitation, including the fusion with neurofeedback BCI systems.

Finally, has contributed to providing open-source tools, which provides a free novel worldwide available toolset comprising multimodal sensing technologies and game training scenarios for at-home use;

In collaboration with clinical centers and research labs of the region of Madeira and mainland Portugal, we realized studies to evaluate RehabNet and its clinical impact. Through RehabNet, we studied how we can reduce cognitive-motor interference in rehabilitation via the appropriate selection of interfaces. We investigated how to improve the ecological validity of combined cognitive-motor training with Rehabcity game, while we also studied Eye-Gaze Patterns in a VR rehabilitation task with both healthy and stroke participants.

By broadening the inclusion criteria for low mobility patients, the RehabNet framework was extended with the development of neurofeedback tools through the utilization of Brain-Computer Interfaces. First we showed that low-cost EEG systems can deliver cost-effective performance levels in motor-imagery training. Then, we showed that VR combined with BCI is able to recruit motor areas to a larger extent by means of a dual motor training and motor imagery paradigm, as well as through motor priming. We also investigated ways to maximize BCI performance of first-time users, and we developed a complete multimodal BCI-VR environment with adaptive performance for motor training.

Finally, clinical studies revealed benefits of longitudinal BCI-VR training in ecologically valid environments when combined with traditional rehabilitation.

Final Remarks and Future Directions

The design of rehabilitation systems which bypass the central nervous system - in the form of BCIs - has inherently major limitations due to its complexity. BCIs have arguably poor usability levels, while cannot be widely used like any other type of computer interface. This is in particular due to their low robustness and reliability, as well as their often long calibration and training sessions, especially in the case of motor-imagery paradigms.
These limiting factors are amplified when the target demographic is consisted of stroke patients which suffer from lesioned parts of the brain, resulting not only in poor motor capability but in mood disorders and depression.
Even though generally high satisfaction is reported with the currently available BCI systems -one could describe it as novelty effect- a clear demand for BCI improvements is strongly reported by end-users and caregivers.

With the impact that current VR technology has, together with high-resolution HMDs, one could argue that the virtual or artificially perceived reality is resulting to higher levels of immersion and pressence, that could change the brain in ways we cannot not yet quantify.
Since current VR can be delivered quite vividly and perceived as real-life experience, the simulated scenarios one can live and interact in such systems

are infinite.

Consequently, the fusion of BCI technology with VR could be described as a controlled dream environment where direct events in the "world" are triggered directly by thought without physical actions, similarly to lucid dreaming. This perceived reality, in a brain level, gives the potential of re-wiring a lesioned brain due to increased sense of body agency or ownership that could possibly result in less chances of malplasticity during a training task. This property, leverages the potential of BCIs significantly, providing a medium where dreams can actually "come true" while the impact is yet underexplored. In that perspective, part of this thesis provided not only the platform but also the insights on how BCI-VR technology can increase the potential of neural interfaces but also with tangible results, increase the quality of life of stroke survivors.

To date, current neural interface technology and BCI could be described in the same way as VR technology was in the 80s-90s - bulky, low resultion, low accuracy, and low immersion equimpment, used only by research labs and big organizations (e.g NASA) - or as the early stages of the internet in the US Department of Defense and the world-wide-web (WWW) in CERN, with Tim Berners-Lee proposal [1] to be described as '*Vague, but exciting*'. In the same way, BCI technology, together with the new discoveries about the brain functioning, will be evolved in a way connecting human and machine, but doing so in a symbiotic manner, synergistically rather antagonistically that is today.

Ultimately, together with past and current research contributions, the fundamental purpose of this thesis is to add a small piece in the board of knowledge towards designing and developing these neuro-aware systems for

[1] `http://info.cern.ch/Proposal.html`

human-machine convergence and symbiosis. This could expand further our perceived knowledge of the functioning of the brain but eventually help significantly to increase the quality of life of those in need.

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Appendices

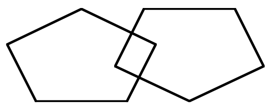
Appendix A

Clinical Assessment Tools

Mini-Mental State Examination (MMSE)

Patient's Name: ____ Date: _____________

Instructions: Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

Interpretation of the MMSE:

Method	Score	Interpretation
Single Cutoff	<24	Abnormal
Range	<21	Increased odds of dementia
	>25	Decreased odds of dementia
Education	21	Abnormal for 8th grade education
	<23	Abnormal for high school education
	<24	Abnormal for college education
Severity	24-30	No cognitive impairment
	18-23	Mild cognitive impairment
	0-17	Severe cognitive impairment

Interpretation of MMSE Scores:

Score	Degree of Impairment	Formal Psychometric Assessment	Day-to-Day Functioning
25-30	Questionably significant	If clinical signs of cognitive impairment are present, formal assessment of cognition may be valuable.	May have clinically significant but mild deficits. Likely to affect only most demanding activities of daily living.
20-25	Mild	Formal assessment may be helpful to better determine pattern and extent of deficits.	Significant effect. May require some supervision, support and assistance.
10-20	Moderate	Formal assessment may be helpful if there are specific clinical indications.	Clear impairment. May require 24-hour supervision.
0-10	Severe	Patient not likely to be testable.	Marked impairment. Likely to require 24-hour supervision and assistance with ADL.

Source:

- Folstein MF, Folstein SE, McHugh PR: "Mini-mental state: A practical method for grading the cognitive state of patients for the clinician." *J Psychiatr Res* 1975;12:189-198.

Stroke Impact Scale

VERSION 3.0

The purpose of this questionnaire is to evaluate how stroke has impacted your health and life. We want to know from **YOUR POINT OF VIEW** how stroke has affected you. We will ask you questions about impairments and disabilities caused by your stroke, as well as how stroke has affected your quality of life. Finally, we will ask you to rate how much you think you have recovered from your stroke.

Stroke Impact Scale

These questions are about the physical problems which may have occurred as a result of your stroke.

1. In the past week, how would you rate the strength of your....	**A lot of strength**	**Quite a bit of strength**	**Some strength**	**A little strength**	**No strength at all**
a. Arm that was most affected by your stroke?	5	4	3	2	1
b. Grip of your hand that was most affected by your stroke?	5	4	3	2	1
c. Leg that was most affected by your stroke?	5	4	3	2	1
d. Foot/ankle that was most affected by your stroke?	5	4	3	2	1

These questions are about your memory and thinking.

2. In the past week, how difficult was it for you to...	**Not difficult at all**	**A little difficult**	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
a. Remember things that people just told you?	5	4	3	2	1
b. Remember things that happened the day before?	5	4	3	2	1
c. Remember to do things (e.g. keep scheduled appointments or take medication)?	5	4	3	2	1
d. Remember the day of the week?	5	4	3	2	1
e. Concentrate?	5	4	3	2	1
f. Think quickly?	5	4	3	2	1
g. Solve everyday problems?	5	4	3	2	1

These questions are about how you feel, about changes in your mood and about your ability to control your emotions since your stroke.

3. In the past week, how often did you...	**None of the time**	**A little of the time**	**Some of the time**	**Most of the time**	**All of the time**
a. Feel sad?	5	4	3	2	1
b. Feel that there is nobody you are close to?	5	4	3	2	1
c. Feel that you are a burden to others?	5	4	3	2	1
d. Feel that you have nothing to look forward to?	5	4	3	2	1
e. Blame yourself for mistakes that you made?	5	4	3	2	1
f. Enjoy things as much as ever?	5	4	3	2	1
g. Feel quite nervous?	5	4	3	2	1
h. Feel that life is worth living?	5	4	3	2	1
i. Smile and laugh at least once a day?	5	4	3	2	1

The following questions are about your ability to communicate with other people, as well as your ability to understand what you read and what you hear in a conversation.

4. In the past week, how difficult was it to...	**Not difficult at all**	**A little difficult**	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
a. Say the name of someone who was in front of you?	5	4	3	2	1
b. Understand what was being said to you in a conversation?	5	4	3	2	1
c. Reply to questions?	5	4	3	2	1
d. Correctly name objects?	5	4	3	2	1
e. Participate in a conversation with a group of people?	5	4	3	2	1
f. Have a conversation on the telephone?	5	4	3	2	1
g. Call another person on the telephone, including selecting the correct phone number and dialing?	5	4	3	2	1

The following questions ask about activities you might do during a typical day.

5. In the past 2 weeks, how difficult was it to...	**Not difficult at all**	**A little difficult**	**Somewhat difficult**	**Very difficult**	**Could not do at all**
a. Cut your food with a knife and fork?	5	4	3	2	1
b. Dress the top part of your body?	5	4	3	2	1
c. Bathe yourself?	5	4	3	2	1
d. Clip your toenails?	5	4	3	2	1
e. Get to the toilet on time?	5	4	3	2	1
f. Control your bladder (not have an accident)?	5	4	3	2	1
g. Control your bowels (not have an accident)?	5	4	3	2	1
h. Do light household tasks/chores (e.g. dust, make a bed, take out garbage, do the dishes)?	5	4	3	2	1
i. Go shopping?	5	4	3	2	1
j. Do heavy household chores (e.g. vacuum, laundry or yard work)?	5	4	3	2	1

The following questions are about your ability to be mobile, at home and in the community.

6. In the past 2 weeks, how difficult was it to...	**Not difficult at all**	**A little difficult**	**Somewhat difficult**	**Very difficult**	**Could not do at all**
a. Stay sitting without losing your balance?	5	4	3	2	1
b. Stay standing without losing your balance?	5	4	3	2	1
c. Walk without losing your balance?	5	4	3	2	1
d. Move from a bed to a chair?	5	4	3	2	1
e. Walk one block?	5	4	3	2	1
f. Walk fast?	5	4	3	2	1
g. Climb one flight of stairs?	5	4	3	2	1
h. Climb several flights of stairs?	5	4	3	2	1
i. Get in and out of a car?	5	4	3	2	1

The following questions are about your ability to use your hand that was MOST AFFECTED by your stroke.

7. In the past 2 weeks, how difficult was it to use your hand that was most affected by your stroke to...	**Not difficult at all**	**A little difficult**	**Somewhat difficult**	**Very difficult**	**Could not do at all**
a. Carry heavy objects (e.g. bag of groceries)?	5	4	3	2	1
b. Turn a doorknob?	5	4	3	2	1
c. Open a can or jar?	5	4	3	2	1
d. Tie a shoe lace?	5	4	3	2	1
e. Pick up a dime?	5	4	3	2	1

The following questions are about how stroke has affected your ability to participate in the activities that you usually do, things that are meaningful to you and help you to find purpose in life.

8. During the past 4 weeks, how much of the time have you been limited in...	**None of the time**	**A little of the time**	**Some of the time**	**Most of the time**	**All of the time**
a. Your work (paid, voluntary or other)	5	4	3	2	1
b. Your social activities?	5	4	3	2	1
c. Quiet recreation (crafts, reading)?	5	4	3	2	1
d. Active recreation (sports, outings, travel)?	5	4	3	2	1
e. Your role as a family member and/or friend?	5	4	3	2	1
f. Your participation in spiritual or religious activities?	5	4	3	2	1
g. Your ability to control your life as you wish?	5	4	3	2	1
h. Your ability to help others?	5	4	3	2	1

9. Stroke Recovery

On a scale of 0 to 100, with 100 representing full recovery and 0 representing no recovery, how much have you recovered from your stroke?

______ 100 Full Recovery

—

______ 90

—

______ 80

—

______ 70

—

______ 60

—

______ 50

—

______ 40

—

______ 30

—

______ 20

—

______ 10

________ 0 No Recovery

Item Clarifications

1. If patient says "I don't have an affected side", then instruct them to score using their perceived weaker side. If they still insist there is no affected, or weaker, side instruct them to score using their dominant side.

4. If patient says s/he does not do any or all of the items listed, code item(s) as *Extremely Difficult.*
   (Item f) If patient does not call but is handed the phone this is OK.
   (Item g) If patient cannot hold a phone book, if they can read it this is OK. This item addresses whether the patient is able to initiate a phone call, look up the number, and dial this number correctly.

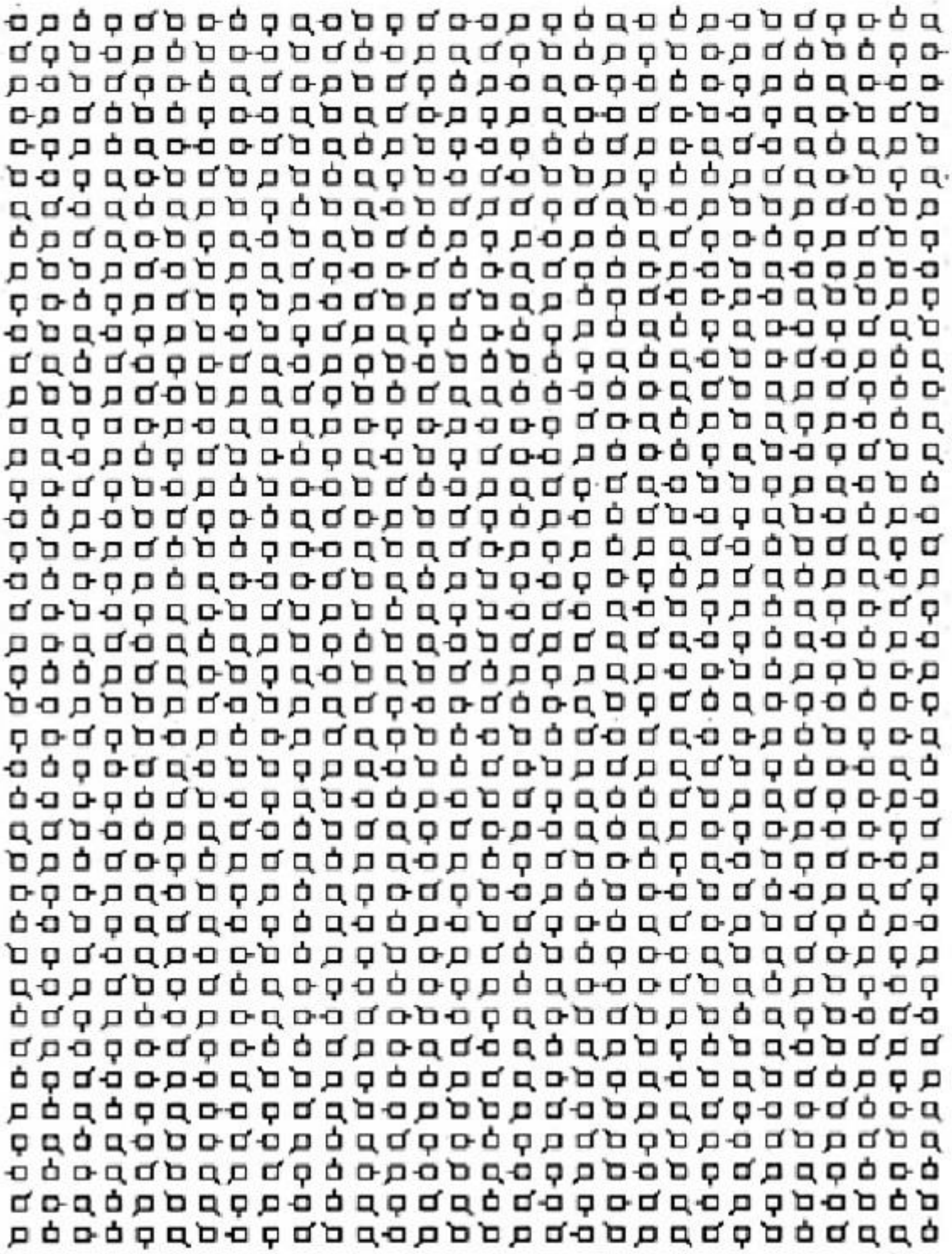
5. If patient says s/he does not do any or all of the items listed, code item(s) as *Cannot do at all.*
   (Item a) If person is on pureed food, even if they feel they could cut the food, code as *Cannot do at All* (1/5/98)
   (Item c) Bathing oneself does not include getting into the tub.
   (Item e) This question is associated with movement. Does the person have the physical ability to get to the bathroom quickly enough?
   (Item f) Losing a little urine/dribbling is considered an accident.
      If person has intermittent catheter and is having no leaking problems code them as per report. (1/5/98)
      If person has an in-dwelling Foley catheter, code as *Cannot do at all.* (1/5/98)
   (Item g) Constipation is not counted here, person has to have an accident.
   (Item i) "Shopping" means any type of shopping and does not include driving.

6. If patient hasn't done any of the items in the past two weeks code as *Cannot do at all.*
   (Item h) If patient hasn't "climbed several flights of stairs" in two weeks, they may be prompted by saying "have you gone up and down one flight of stairs a couple of times in a row." If they still say they have not done it then they must be coded as *Cannot do at all.*
   (Item i) If the patient wants to know what kind of car say "your car" or "the car you ride in most."

7. If patient says "I don't have an affected side", then instruct them to score using their perceived weaker side. If they still insist there is no affected, or weaker, side instruct them to score using their dominant side.
   (Item a) If the patient says s/he has not been to the grocery store say "have you carried anything heavy with that hand."
   (Item d) This item is to tie a shoelace/bow using both hands.

8. If patient does not do any of the specific items (and has never done), code interference as *None of the time.*

TEST DE TOULOUSE PIÉRON



ADDENBROOKE'S COGNITIVE EXAMINATION - ACE-R

Final Revised Version A (2005)

Name : Date of birth : Hospital no. : *Addressograph*	Date of testing: .... /........ /....... Tester's name: .... Age at leaving full-time education: .... Occupation: .... Handedness: ....

ORIENTATION

➢ Ask: What is the	Day	Date	Month	Year	Season	[Score 0-5]
➢ Ask: Which	Building	Floor	Town	County	Country	[Score 0-5]

REGISTRATION

➢ Tell: 'I'm going to give you three words and i'd like you to repeat after me: lemon, key and ball'. After subject repeats, say 'Try to remember them because i'm going to ask you later'. Score only the first trial (repeat 3 times if necessary).

Register number of trials ....

[Score 0-3]

ATTENTION & CONCENTRATION

➢ Ask the subject: ' could you take 7 away from a 100? After the subject responds, ask him or her to take away another 7 to a total of 5 subtractions. If subject make a mistake, carry on and check the subsequent answer (i.e. 93, 84, 77, 70, 63 -score 4)

Stop after five subtractions (93, 86, 79, 72, 65). ....

➢ Ask: 'could you please spell **WORLD** for me? Then ask him/her to spell it backwards:

....

[Score 0-5]

(for the best performed task)

ATTENTION & ORIENTATION

MEMORY - Recall

➢ Ask: 'Which 3 words did I ask you to repeat and remember?'

....

[Score 0-3]

MEMORY - Anterograde Memory

➢ Tell: ' I'm going to give you a name and address and I'd like you to repeat after me. We'll be doing that 3 times, so you have a chance to learn it. I'll be asking you later'

Score only the third trial

[Score 0-7]

	1st Trial	2nd Trial	**3rd Trial**
Harry Barnes	....	....	....
73 Orchard Close	....	....	....
Kingsbridge	....	....	....
Devon	....	....	....

MEMORY - Retrograde Memory

➢ Name of current Prime Minister ....
➢ Name of the woman who was Prime Minister ....
➢ Name of the USA president ....
➢ Name of the USA president who was assassinated in the 1960's ....

[Score 0 -4]

MEMORY

VERBAL FLUENCY - Letter 'P' and animals

➢ **Letters**

Say: 'I'm going to give you a letter of the alphabet and I'd like you to generate as many words as you can beginning with that letter, but not names of people or places. Are you ready? You've got a minute and the letter is P'

[Score 0 - 7]

total	correct
>17	7
14-17	6
11-13	5
8-10	4
6-7	3
4-5	2
2-3	1
<2	0

➢ **Animals**

Say: 'Now can you name as many animals as possible, beginning with any letter?

[Score 0 - 7]

total	correct
>21	7
17-21	6
14-16	5
11-13	4
9-10	3
7-8	2
5-6	1
<5	0

FLUENCY

LANGUAGE - Comprehension

➢ Show written instruction:

[Score 0-1]

Close your eyes

➢ 3 stage command:
'Take the paper in your right hand. Fold the paper in half. Put the paper on the floor'

[Score 0-3]

LANGUAGE - Writing

➢ Ask the subject to make up a sentence and write it in the space below:
Score 1 if sentence contains a subject and a verb (see guide for examples)

[Score 0-1]

LANGUAGE

LANGUAGE - Repetition

- Ask the subject to repeat:**' hippopotamus'; 'eccentricity; 'unintelligible'; 'statistician'**

Score 2 if all correct; 1 if 3 correct; 0 if 2 or less.

[Score 0-2]

- Ask the subject to repeat: **'Above, beyond and below'**

[Score 0-1]

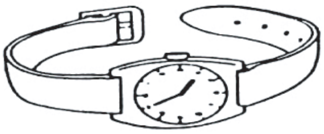
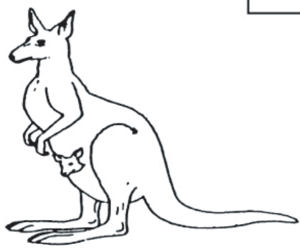
- Ask the subject to repeat: **'No ifs, ands or buts'**

[Score 0-1]

LANGUAGE - Naming

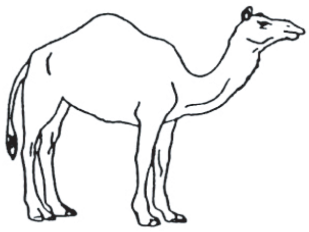
- Ask the subject to name the following pictures:

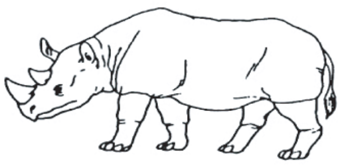
[Score 0-2] pencil + watch

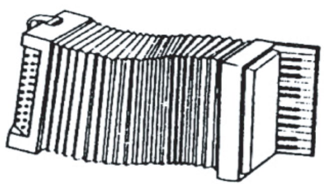
[Score 0-10]







LANGUAGE - Comprehension

- Using the pictures above, ask the subject to:
  - Point to the one which is associated with the monarchy ____________
  - Point to the one which is a marsupial ____________
  - Point to the one which is found in the Antarctic ____________
  - Point to the one which has a nautical connection ____________

[Score 0-4]

L A N G U A G E

LANGUAGE - Reading

➢ Ask the subject to read the following words: [Score 1 only if all correct]

[Score 0-1]

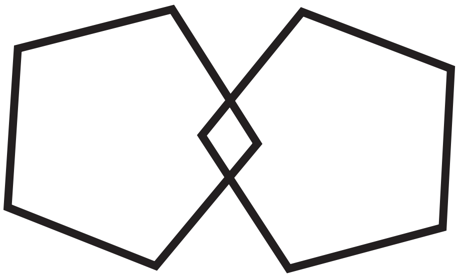
sew
pint
soot
dough
height

L A N G U A G E

VISUOSPATIAL ABILITIES

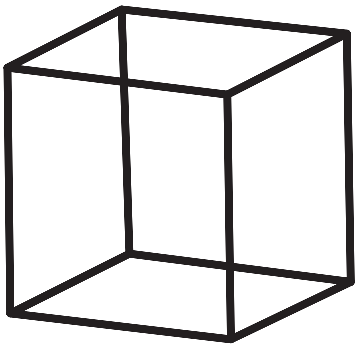
➢ Overlapping pentagons: Ask the subject to copy this diagram:

[Score 0-1]



➢ Wire cube : Ask the subject to copy this drawing (for scoring, see instructions guide)

[Score 0-2]



➢ Clock: Ask the subject to draw a clock face with numbers and the hands at ten past five.
(for scoring see instruction guide: circle = 1, numbers = 2, hands = 2 if all correct)

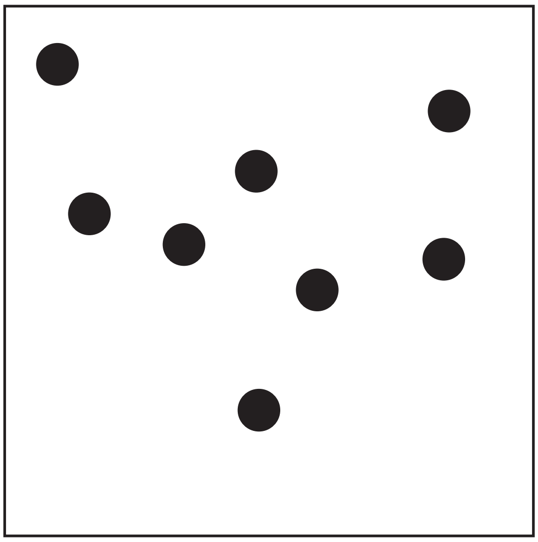
[Score 0-5]

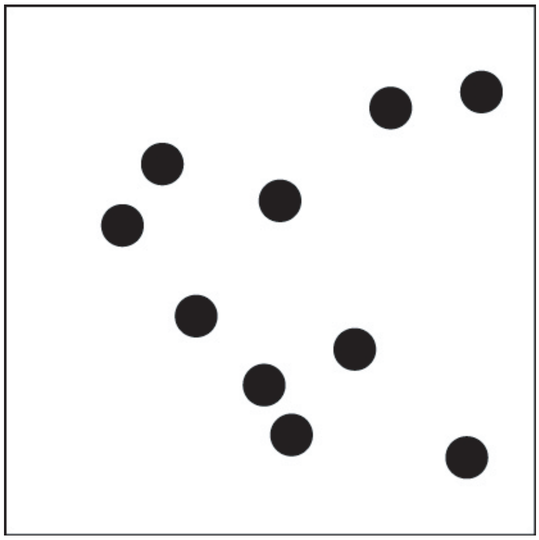
V I S U O S P A T I A L

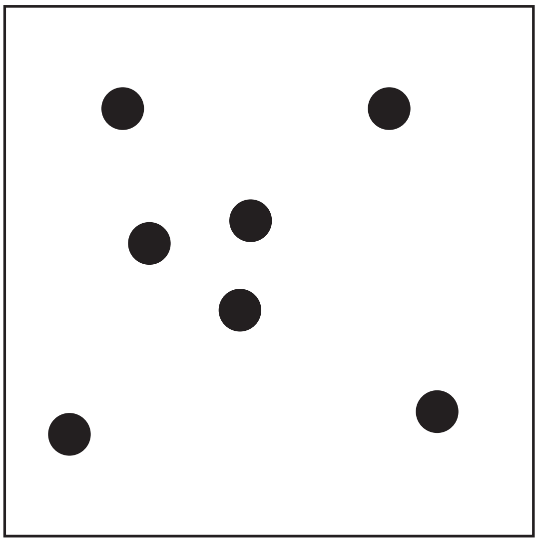
PERCEPTUAL ABILITIES

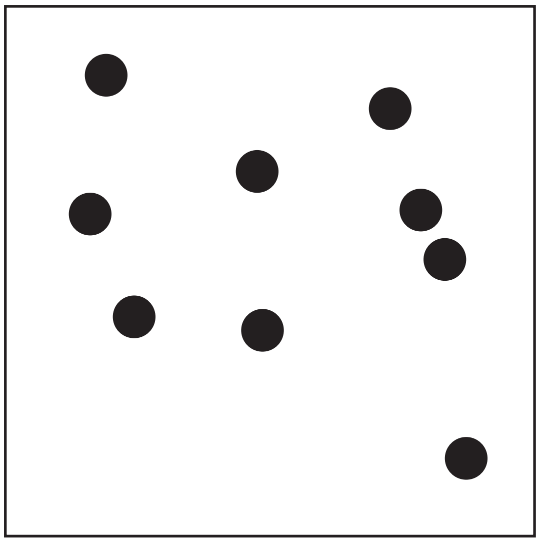
- Ask the subject to count the dots without pointing them

[Score 0-4]









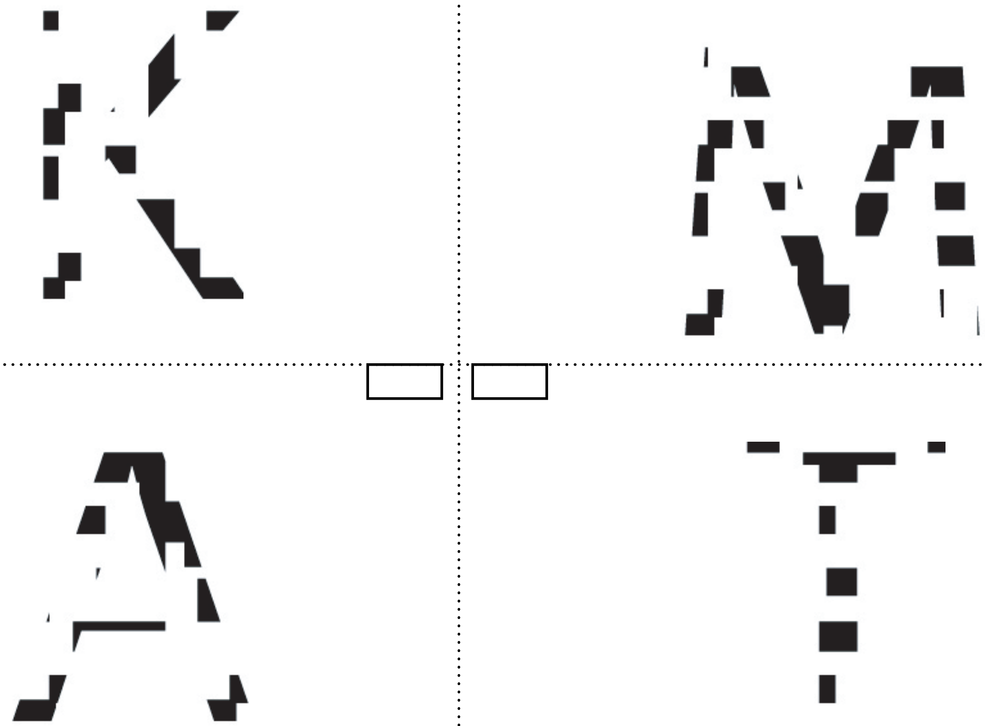
VISUOSPATIAL

PERCEPTUAL ABILITIES

VISUOSPATIAL

➢ Ask the subject to identify the letters

[Score 0-4]



RECALL

MEMORY

➢ Ask “Now tell me what you remember of that name and address we were repeating at the beginning’”

Harry Barnes	………… …………	[Score 0-7]
73 Orchard Close	……. ………… …………	
Kingsbridge	…………	
Devon	…………	

RECOGNITION

➢ This test should be done if subject failed to recall one or more items. If all items were recalled, skip the test and score 5. If only part is recalled start by ticking items recalled in the shadowed column on the right hand side. Then test not recalled items by telling “ok, I’ll give you some hints: was the name X, Y or Z?” and so on. Each recognised item scores one point which is added to the point gained by recalling.

[Score 0-5]

Jerry Barnes		Harry Barnes		Harry Bradford		recalled	
37		73		76		recalled	
Orchard Place		Oak Close		Orchard Close		recalled	
Oakhampton		Kingsbridge		Dartington		recalled	
Devon		Dorset		Somerset		recalled	

General Scores

SCORE

MMSE	/30
ACE-R	/100

Subscores

Attention and Orientation	/18
Memory	/26
Fluency	/14
Language	/26
Visuospatial	/16

Normative values based on 63 controls aged 52-75 and 142 dementia patients aged 46-86

Cut-off <88 gives 94% senstivity and 89% specificity for dementia

Cut-off <82 gives 84% sensitivity and 100% specificity for dementia

Evaluation Stage:	Date:
Subject:	
Hist nr.:	

FUGL-MEYER ASSESSMENT

Motor Function UPPER EXTREMITY (66 points)

A- SHOULDER/ ELBOW/ FOREARM	
I. REFLEX ACTIVITY	
Flexors - Biceps and finger flexion reflex	
Extensors – Triceps reflex	
II. a. FLEXOR SYNERGY	
Shoulder retraction	
Shoulder elevation	
Shoulder abduction	
Shoulder external rotation	
Elbow flexion	
Forearm supination	
II. b. EXTENSOR SYNERGY	
Shoulder adduction/ internal rotation	
Elbow extension	
Forearm pronation	
III.	
Hand movement to lumbar spine	
Shoulder flexion 0-90º	
Forearm supination/ pronation (elbow at 90º, shoulder at 0º)	
IV.	
Shoulder abduction 0º-90º	
Shoulder flexion 90º-180º	
Forearm supination/ pronation (elbow at 0º)	
V. NORMAL REFLEX ACTIVITY	
Biceps, triceps and finger flexors reflexes	
B- WRIST	
Wrist stability with elbow at 90º (wrist extension against resistance)	

A.I
0: no reflex activity
2: reflex activity in flexors/ extensors
Max score in I: 4 points

A.II
0: cannot perform
1: performs partially
2: performs fully
Max score in II: 18 points

A.III
Hand move to lumbar spine
0: cannot perform
1: hand passes the anterior-superior iliac spine
2: performs fully
Shoulder flexion
0: cannot perform, or at the beginning of the movement the arm is already abducted or the elbow flexed
1: in a later phase of the movement, shoulder abduction or elbow flexion occurs
2: performs fully
Forearm supination/ pronation
0: cannot perform, or correct position of the shoulder and the elbow cannot be obtained
1: active supination/ pronation in a limited range, but with shoulder and elbow well positioned
2: performs fully
Max score in III: 6 points

A.IV
Shoulder abduction
0: cannot perform, or at the beginning the elbow is already flexed or forearm is deviated from pronated position
1: performs partially, or during the motion the elbow is flexed
2: performs fully
Shoulder flexion
0: cannot perform, or at the beginning of the movement the arm is already abducted or the elbow flexed
1: in a later phase of the movement, shoulder abduction or elbow flexion occurs
2: performs fully
Forearm supination/ pronation
0: cannot perform, or correct position of the shoulder and the elbow cannot be obtained
1: active supination/ pronation in a limited range, but with shoulder and elbow well positioned
2: performs fully
Max score in IV: 6 points

A.V
Performed only if score = 6 in stage IV
0: at least 2 of the 3 phasic reflexes are markedly hyperactive
1: one reflex markedly hyperactive or at least 2 reflexes lively
2: no more than one reflex lively and no reflexes markedly hyperactive
Max score in V: 2 points

Fugl-Meyer AR, Jaasko L, Leyman I, Olsson S, Steglind S (1975) The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. Scand J Rehabil Med 7: 13-31

Wrist flexion/ extension with elbow at 90º	
Wrist stability with elbow at 0º (wrist extension against resistance)	
Wrist flexion/ extension with elbow at 0º	
Wrist circumduction	
C- HAND	
Fingers mass flexion	
Fingers mass extension	
Grasp a (extension of mcp joints and flexion of proximal and distal joints)	
Grasp b (thumb adduction, paper interposed)	
Grasp c (thumb opposition against the second finger, pencil interposed)	
Grasp d (cylinder)	
Grasp e (tennis ball)	
D- COORDINATION/ SPEED	
Finger-to-nose tremor	
Finger-to-nose dysmetria	
Finger-to-nose speed	
TOTAL	

B

Elbow 90º - wrist stability
0: no dorsiflexion of the wrist
1: dorsiflexion can be performed but no resistance can be taken
2: performs fully
Elbow 90º - wrist flexion/ extension
0: cannot perform
1: performs partially
2: performs fully
Elbow 0º - wrist stability
0: no dorsiflexion of the wrist
1: dorsiflexion can be performed but no resistance can be taken
2: performs fully
Elbow 0º - wrist flexion/ extension
0: cannot perform
1: performs partially
2: performs fully
Circumduction
0: cannot perform
1: jerky motion or incomplete circumduction
2: performs fully
Max score in B: 10 points

C

Finger mass flexion
0: no flexion
1: some, but no full active finger flexion
2: full active flexion
Finger mass extension
0: no extension
1: some, but no full active finger extension
2: full active extension
Grasp a
0: the position cannot be acquired
1: the grasp is weak
2: the grasp can be maintained against resistance
Grasp b-e
0: cannot perform
1: object kept in place but not against a slight tug
2: object is held well against a tug
Max score in C: 14 points

D

Tremor
0: marked tremor
1: slight tremor
2: no tremor
Dysmetria
0: pronounced or unsystematic dysmetria
1: slight and systematic dysmetria
2: no dysmetria
Speed
0: the task repeated 5 times is at least 6 seconds slower on the affected side
1: 2 to 5 seconds slower on the affected side
2: less than 2 seconds difference
Max score in D: 6 points

Fugl-Meyer AR, Jaasko L, Leyman I, Olsson S, Steglind S (1975) The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. Scand J Rehabil Med 7: 13-31

THE BARTHEL INDEX

Patient Name: ______________________________

Rater Name: ______________________________

Date: ______________________________

Activity	**Score**
FEEDING 0 = unable 5 = needs help cutting, spreading butter, etc., or requires modified diet 10 = independent	______
BATHING 0 = dependent 5 = independent (or in shower)	______
GROOMING 0 = needs to help with personal care 5 = independent face/hair/teeth/shaving (implements provided)	______
DRESSING 0 = dependent 5 = needs help but can do about half unaided 10 = independent (including buttons, zips, laces, etc.)	______
BOWELS 0 = incontinent (or needs to be given enemas) 5 = occasional accident 10 = continent	______
BLADDER 0 = incontinent, or catheterized and unable to manage alone 5 = occasional accident 10 = continent	______
TOILET USE 0 = dependent 5 = needs some help, but can do something alone 10 = independent (on and off, dressing, wiping)	______
TRANSFERS (BED TO CHAIR AND BACK) 0 = unable, no sitting balance 5 = major help (one or two people, physical), can sit 10 = minor help (verbal or physical) 15 = independent	______
MOBILITY (ON LEVEL SURFACES) 0 = immobile or < 50 yards 5 = wheelchair independent, including corners, > 50 yards 10 = walks with help of one person (verbal or physical) > 50 yards 15 = independent (but may use any aid; for example, stick) > 50 yards	______
STAIRS 0 = unable 5 = needs help (verbal, physical, carrying aid) 10 = independent	______

TOTAL (0–100): _____

The Barthel ADL Index: Guidelines

1. The index should be used as a record of what a patient does, not as a record of what a patient could do.
2. The main aim is to establish degree of independence from any help, physical or verbal, however minor and for whatever reason.
3. The need for supervision renders the patient not independent.
4. A patient's performance should be established using the best available evidence. Asking the patient, friends/relatives and nurses are the usual sources, but direct observation and common sense are also important. However direct testing is not needed.
5. Usually the patient's performance over the preceding 24-48 hours is important, but occasionally longer periods will be relevant.
6. Middle categories imply that the patient supplies over 50 per cent of the effort.
7. Use of aids to be independent is allowed.

References

Mahoney FI, Barthel D. “Functional evaluation: the Barthel Index.”
Maryland State Medical Journal 1965;14:56-61. Used with permission.

Loewen SC, Anderson BA. “Predictors of stroke outcome using objective measurement scales.”
***Stroke.* 1990;21:78-81.**

Gresham GE, Phillips TF, Labi ML. “ADL status in stroke: relative merits of three standard indexes.”
***Arch Phys Med Rehabil.* 1980;61:355-358.**

Collin C, Wade DT, Davies S, Horne V. “The Barthel ADL Index: a reliability study.”
***Int Disability Study.*1988;10:61-63.**

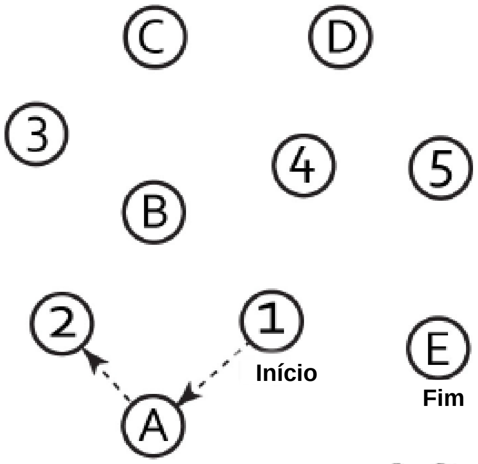
Copyright Information

MONTREAL COGNITIVE ASSESSMENT (MOCA)

VERSÃO PORTUGUESA 7.2 – VERSÃO ALTERNATIVA

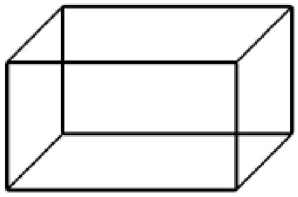
Nome: ____________________ **Idade:** __________
Género: __________ **Data de Nascimento:** __________
Escolaridade: _____ **Data de Avaliação:** ____________

VISUO-ESPACIAL / EXECUTIVA



[ ]

Copiar o paralelepípedo



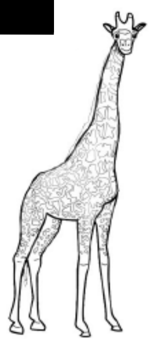
[ ]

Desenhar um Relógio (quatro e cinco) (3 pontos)

[ ] Contorno [ ] Números [ ] Ponteiros

Pontos ___/5

NOMEAÇÃO



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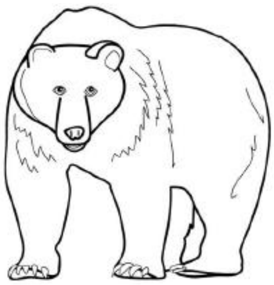

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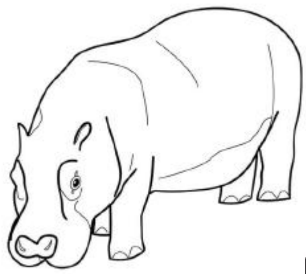

[ ]

___/3

MEMÓRIA

Leia a lista de palavras.
O sujeito deve repeti-la.
Realize dois ensaios.
Solicite a evocação da lista
5 minutos mais tarde.

	Trator	Ananás	Guitarra	Cama	Verde
1º ensaio					
2º ensaio					

Sem Pontuação

ATENÇÃO

Leia a sequência de números. (1 número/segundo)

O sujeito deve repetir a sequência. [ ] **3 2 9 6 5**
O sujeito deve repetir a sequência na ordem inversa. [ ] **8 5 2**

___/2

Leia a série de letras (1 letra/segundo). O sujeito deve bater com a mão cada vez que for dita a letra A. Não se atribuem pontos se ≥ 2 erros.

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

___/1

Subtrair de 7 em 7 começando em 90. [ ] **83** [ ] **76** [ ] **69** [ ] **62** [ ] **55**

4 ou 5 subtracções correctas: **3 pontos;** 2 ou 3 correctas: **2 pontos;** 1 correcta: **1 ponto;** 0 correctas: **0 pontos**

___/3

LINGUAGEM

Repetir: Com muito vento e escuridão, os pássaros podem voar contra janelas fechadas. [ ] **A avó, atenciosa, enviou-lhes mercearias há uma semana.** [ ]

___/2

Fluência verbal: Dizer o maior número possível de palavras que comecem pela letra "D" (1 minuto). [ ] ____ (N ≥ 11 Palavras)

___/1

ABSTRACÇÃO

Semelhança p.ex. entre cenoura e batata = vegetais [ ] **diamante - rubi** [ ] **canhão - espingarda**

___/2

EVOCAÇÃO DIFERIDA

	Trator	Ananás	Guitarra	Cama	Verde	
Deve recordar as palavras **SEM PISTAS**	[ ]	[ ]	[ ]	[ ]	[ ]	Pontuação apenas para evocação **SEM PISTAS**
Opcional — Pista de categoria						
Opcional — Pista de escolha múltipla						

___/5

ORIENTAÇÃO

[ ] Dia do mês [ ] Mês [ ] Ano [ ] Dia da semana [ ] Lugar [ ] Localidade

___/6

Adapted by : Z. Nasreddine MD, N. Phillips PhD, H. Chertkow MD

Examinador: ______________

TOTAL ___/30

Versão Portuguesa: Freitas, S., Simões, M. R., Santana, I., Martins, C. & Nasreddine, Z. (2013). *Montreal Cognitive Assessment (MoCA): Versão 2*. Coimbra: Faculdade de Psicologia e de Ciências da Educação da Universidade de Coimbra.

Modified Ashworth Scale

The Modified Ashworth Scale (MAS) measures resistance during passive soft-tissue stretching. It is a quick and easy measure that can help assess the efficacy of treatment. The following conventions prevail:

- The MAS is performed in the supine position (this will garner the most accurate and the lowest score as any tension anywhere in the body will increase spasticity)
- Because spasticity is "velocity dependent" (the faster the limb is moved, the more spasticity is encountered), the MAS is performed while moving the limb at the "speed of gravity"; this is defined as the same speed at which a non-spastic limb would naturally drop (fairly fast)
- The test is performed a maximum of three times for each joint; if more than three times, the short-term effect of a stretch can influence the score
- The MAS is performed prior to goniometric testing; goniometric testing provides a stretch, and the short-term effect of a stretch can influence the score

Scoring

0 = Normal tone, no increase in tone
1 = Slight increase in muscle tone, manifested by a catch and release or minimal resistance at the end of the range of motion (ROM) when the affected part(s) is moved in flexion or extension
1+ = Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2 = More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3 = Considerable increase in muscle tone, passive movement difficult
4 = Affected part(s) rigid in flexion or extension

Positions

The positions used for an MAS assessment are as follows:

Score______Elbow. *Start position:* Elbow fully flexed, forearm neutral. Movement: Extend elbow from maximum possible flexion to maximum possible extension. (Triceps would be in the same position, opposite direction.)

Score______Wrist. *Start position:* Elbow as straight as possible, forearm pronated. Movement: Extend the patient's wrist from maximum possible flexion to maximum possible extension.

Score______Fingers. *Start position:* Elbow as straight as possible, forearm neutral. All fingers are done at once. Movement: Extend the patient's fingers from maximum possible flexion to maximum possible extension.

Score______Thumb. *Start position:* Elbow as straight as possible, forearm neutral, wrist neutral. Movement: Extend the thumb from maximum possible flexion (thumb against index finger) to maximum possible extension (in anatomical position, "abducted").

Score______Hamstrings. *Start position:* Prone so that ankle falls beyond end of the plinth, hip in neutral rotation. Movement: Extend the patient's knee from maximum possible flexion to maximum possible extension

Score______Quadriceps. *Start position:* Prone so that ankle falls beyond end of the plinth, hip in neutral rotation. Movement: Flex the patient's limb from maximum possible flexion to maximum possible extension

Score______Gastrocnemius. *Start position:* Supine, ankle plantarflexed, hip in neutral rotation and flexion. Movement: Dorsiflex the patient's ankle from maximum possible plantarflexion to maximum possible dorsiflexion not more than three consecutive times and rate the muscle tone.

Score______Soleus. *Start position:* Supine, ankle plantarflexed, hip in neutral rotation and flexion and with the knee flexed to ~15°. Movement: Dorsiflex the patient's ankle from maximum possible plantarflexion to maximum possible dorsiflexion.

Appendix B

Usability Assessment Tools

Vividness of Movement Imagery Questionnaire-2

Name: **Age:**

Gender: **Sport:**

Level at which sport is played at (e.g., Recreational, Club, University, National, International, Professional)

Years spent participating in this sport competitively:

Movement imagery refers to the ability to imagine a movement. The aim of this questionnaire is to determine the vividness of your movement imagery. The items of the questionnaire are designed to bring certain images to your mind. You are asked to rate the vividness of each item by reference to the 5-point scale. After each item, circle the appropriate number in the boxes provided. The first column is for an image obtained watching yourself performing the movement from an external point of view (External Visual Imagery), and the second column is for an image obtained from an internal point of view, as if you were looking out through your own eyes whilst performing the movement (Internal Visual Imagery). The third column is for an image obtained by feeling yourself do the movement (Kinaesthetic imagery). Try to do each item separately, independently of how you may have done other items. Complete all items from an external visual perspective and then return to the beginning of the questionnaire and complete all of the items from an internal visual perspective, and finally return to the beginning of the questionnaire and complete the items while feeling the movement. The three ratings for a given item may not in all cases be the same. For all items please have your eyes CLOSED.

Think of each of the following acts that appear on the next page, and classify the images according to the degree of clearness and vividness as shown on the RATING SCALE.

RATING SCALE. The image aroused by each item might be:

Perfectly clear and as vivid (as normal vision or feel of movement)	……………	RATING 1
Clear and reasonably vivid	……………	RATING 2
Moderately clear and vivid	……………	RATING 3
Vague and dim	……………	RATING 4
No image at all, you only "know" that you are thinking of the skill.	……………	RATING 5

	Watching yourself performing the movement (External Visual Imagery)						Looking through your own eyes whilst performing the movement (Internal Visual Imagery)						Feeling yourself do the movement (Kinaesthetic Imagery)				
Item	Perfectly clear and vivid as normal vision	Clear and reasonably vivid	Moderately clear and vivid	Vague and dim	No image at all, you only know that you are thinking of the skill		Perfectly clear and vivid as normal vision	Clear and reasonably vivid	Moderately clear and vivid	Vague and dim	No image at all, you only know that you are thinking of the skill		Perfectly clear and vivid as normal feel of movement	Clear and reasonably vivid	Moderately clear and vivid	Vague and dim	No image at all, you only know that you are thinking of the skill
1.Walking	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
2.Running	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
3.Kicking a stone	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
4.Bending to pick up a coin	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
5.Running up stairs	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
6.Jumping sideways	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
7.Throwing a stone into water	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
8.Kicking a ball in the air	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
9.Running downhill	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
10.Riding a bike	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
11.Swinging on a rope	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
12.Jumping off a high wall	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5

1. Please indicate if you have a preference for using a particular visual imagery perspective on this scale (if you have no preference then circle 5):

0	1	2	3	4	5	6	7	8	9	10
Strong preference internal			Moderate preference internal		No preference		Moderate preference external			Strong preference external

2. Please indicate on the following questions the extent to which you "switched" between imagery perspectives, when completing the two visual columns of the adapted VMIQ:

a) When completing the *watching yourself do it* (External Visual Imagery) column, what perspective did you use?

0	1	2	3	4	5	6	7	8	9	10
Completely internal perspective		minimal switching to an external perspective			switched regularly			minimal switching to an internal perspective		completely external perspective

b) When completing the *looking through your own eyes* (Internal Visual Imagery) column, what perspective did you use?

0	1	2	3	4	5	6	7	8	9	10
Completely internal perspective		minimal switching to an external perspective			switched regularly			minimal switching to an internal perspective		completely external perspective

3. When completing the two visual imagery columns please specify if you used kinaesthetic imagery at the same time as the designated visual imagery perspective:

EVI

0	1	2	3	4	5	6	7	8	9	10
No kinaesthetic imagery use										high kinaesthetic imagery use

IVI

0	1	2	3	4	5	6	7	8	9	10
No kinaesthetic imagery use										high kinaesthetic imagery use

4. If you used kinaesthetic imagery at the same time as the designated visual perspective please denote (Using the numbers 3 = most often, 1 = least often) the order in which visual and kinaesthetic imagery were used

EVI

Visual and Kinaesthetic imagery at the same time ______
Visual then kinaesthetic imagery ______
Kinaesthetic then visual imagery ______

IVI

Visual and Kinaesthetic imagery at the same time ______
Visual then kinaesthetic imagery ______
Kinaesthetic then visual imagery ______

5. On <u>one</u> of the diagrams below, please draw an arrow to illustrate where you imaged from most of the time, when completing the external visual imagery column.

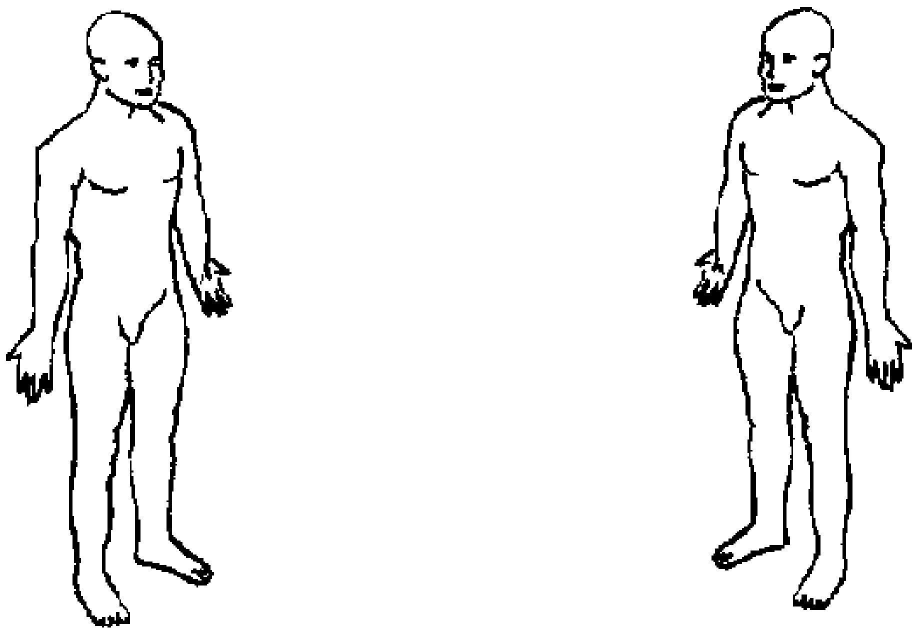

Figure 8.6

NASA Task Load Index

Hart and Staveland's NASA Task Load Index (TLX) method assesses work load on five 7-point scales. Increments of high, medium and low estimates for each point result in 21 gradations on the scales.

Name	Task	Date

Mental Demand — How mentally demanding was the task?

Very Low — Very High

Physical Demand — How physically demanding was the task?

Very Low — Very High

Temporal Demand — How hurried or rushed was the pace of the task?

Very Low — Very High

Performance — How successful were you in accomplishing what you were asked to do?

Perfect — Failure

Effort — How hard did you have to work to accomplish your level of performance?

Very Low — Very High

Frustration — How insecure, discouraged, irritated, stressed, and annoyed wereyou?

Very Low — Very High

PRESENCE QUESTIONNAIRE

(Witmer & Singer, Vs. 3.0, Nov. 1994)*
Revised by the UQO Cyberpsychology Lab (2004)

Characterize your experience in the environment, by marking an "X" in the appropriate box of the 7-point scale, in accordance with the question content and descriptive labels. Please consider the entire scale when making your responses, as the intermediate levels may apply. Answer the questions independently in the order that they appear. Do not skip questions or return to a previous question to change your answer.

WITH REGARD TO THE EXPERIENCED ENVIRONMENT

1. How much were you able to control events?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT COMPLETELY

2. How responsive was the environment to actions that you initiated (or performed)?

|________|________|________|________|________|________|________|
NOT RESPONSIVE MODERATELY RESPONSIVE COMPLETELY RESPONSIVE

3. How natural did your interactions with the environment seem?

|________|________|________|________|________|________|________|
EXTREMELY ARTIFICIAL BORDERLINE COMPLETELY NATURAL

4. How much did the visual aspects of the environment involve you?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT COMPLETELY

5. How natural was the mechanism which controlled movement through the environment?

|________|________|________|________|________|________|________|
EXTREMELY ARTIFICIAL BORDERLINE COMPLETELY NATURAL

6. How compelling was your sense of objects moving through space?

|________|________|________|________|________|________|________|
NOT AT ALL MODERATELY VERY
COMPELLING COMPELLING

7. How much did your experiences in the virtual environment seem consistent with your real world experiences?

|________|________|________|________|________|________|________|
NOT MODERATELY VERY
CONSISTENT CONSISTENT CONSISTENT

8. Were you able to anticipate what would happen next in response to the actions that you performed?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT COMPLETELY

9. How completely were you able to actively survey or search the environment using vision?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT COMPLETELY

10. How compelling was your sense of moving around inside the virtual environment?

|________|________|________|________|________|________|________|
NOT MODERATELY VERY
COMPELLING COMPELLING COMPELLING

11. How closely were you able to examine objects?

|________|________|________|________|________|________|________|
NOT AT ALL PRETTY VERY
CLOSELY CLOSELY

12. How well could you examine objects from multiple viewpoints?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT EXTENSIVELY

13. How involved were you in the virtual environment experience?

|________|________|________|________|________|________|________|

NOT INVOLVED — MILDLY INVOLVED — COMPLETELY ENGROSSED

NOT INVOLVED	MILDLY INVOLVED	COMPLETELY ENGROSSED

14. How much delay did you experience between your actions and expected outcomes?

|________|________|________|________|________|________|________|

NO DELAYS	MODERATE DELAYS	LONG DELAYS

15. How quickly did you adjust to the virtual environment experience?

|________|________|________|________|________|________|________|

NOT AT ALL	SLOWLY	LESS THAN ONE MINUTE

16. How proficient in moving and interacting with the virtual environment did you feel at the end of the experience?

|________|________|________|________|________|________|________|

NOT PROFICIENT	REASONABLY PROFICIENT	VERY PROFICIENT

17. How much did the visual display quality interfere or distract you from performing assigned tasks or required activities?

|________|________|________|________|________|________|________|

NOT AT ALL	INTERFERED SOMEWHAT	PREVENTED TASK PERFORMANCE

18. How much did the control devices interfere with the performance of assigned tasks or with other activities?

|________|________|________|________|________|________|________|

NOT AT ALL	INTERFERED SOMEWHAT	INTERFERED GREATLY

19. How well could you concentrate on the assigned tasks or required activities rather than on the mechanisms used to perform those tasks or activities?

|________|________|________|________|________|________|________|

NOT AT ALL	SOMEWHAT	COMPLETELY

IF THE VIRTUAL ENVIRONMENT INCLUDED SOUNDS:

20. How much did the auditory aspects of the environment involve you?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT COMPLETELY

21. How well could you identify sounds?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT COMPLETELY

22. How well could you localize sounds?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT COMPLETELY

IF THE VIRTUAL ENVIRONMENT INCLUDED HAPTIC (SENSE OF TOUCH):

23. How well could you actively survey or search the virtual environment using touch?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT COMPLETELY

24. How well could you move or manipulate objects in the virtual environment?

|________|________|________|________|________|________|________|
NOT AT ALL SOMEWHAT EXTENSIVELY

Last version : March 2013

*Original version : Witmer, B.G. & Singer. M.J. (1998). Measuring presence in virtual environments: A presence questionnaire. *Presence : Teleoperators and Virtual Environments*, *7*(3), 225-240. Revised factor structure: Witmer, B.J., Jerome, C.J., & Singer, M.J. (2005). The factor structure of the Presence Questionnaire. *Presence, 14*(3) 298-312.

Questionnaire sur l'État de Présence (QÉP)
Laboratoire de Cyberpsychologie de l'UQO

Validation of the French-Canadian version developed by the UQO Cyberpsychology Lab:

- 101 participants completed the questionnaire following an immersion in a virtual environment;
- Cronbach's Alpha = .84
- Now 19 items (for VEs without sound/touch) et 24 items (for VEs with sounds/touch)

Scoring :

Total : Items 1 to 19 (reverse items 14, 17, 18)

- « Realism » : Items 3 + 4 + 5 + 6 + 7 + 10 + 13
- « Possibility to act » : Items 1 + 2 + 8 + 9
- « Quality of interface » : Items (all reversed) 14 + 17 + 18
- « Possibility to examine » : Items 11 + 12 + 19
- « Self-evaluation of performance » : Items 15 + 16
- « Sounds* » : Items 20 + 21 + 22
- « Haptic* » : Items 23 + 24

* NOTE : Scoring of « *sounds* » and « *haptic* » are not part of the factor analysis of the French version.

Norms (French version) :

	Moyenne	**Écart type**
Total	104.39	18.99
« Realism »	29.45	12.04
« Possibility to act »	20.76	6.01
« Quality of interface »	15.37	5.15
« Possibility to examine»	15.38	4.90
« Auto-évaluation de la performance »	11.00	2.87

Last version : March 2013

*Original version : Witmer, B.G. & Singer. M.J. (1998). Measuring presence in virtual environments: A presence questionnaire. *Presence : Teleoperators and Virtual Environments*, *7*(3), 225-240. The factor structure of the Presence Questionnaire. *Presence, 14*(3) 298-312. Revised factor structure: Witmer, B.J., Jerome, C.J., & Singer, M.J. (2005). The factor structure of the Presence Questionnaire. *Presence, 14*(3) 298-312.

System Usability Scale

	Strongly disagree 1	2	3	4	Strongly agree 5
1. I think that I would like to use this system frequently	1	2	3	4	5
2. I found the system unnecessarily complex	1	2	3	4	5
3. I thought the system was easy to use	1	2	3	4	5
4. I think that I would need the support of a technical person to be able to use this system	1	2	3	4	5
5. I found the various functions in this system were well integrated	1	2	3	4	5
6. I thought there was too much inconsistency in this system	1	2	3	4	5
7. I would imagine that most people would learn to use this system very quickly	1	2	3	4	5
8. I found the system very cumbersome to use	1	2	3	4	5
9. I felt very confident using the system	1	2	3	4	5
10. I needed to learn a lot of things before I could get going with this system	1	2	3	4	5

Gamer Dedication (GD)

The 15 Factors of Classification and associated weightings (ranked according to weight)

Factor	Weighting
1. Play games over many long sessions	10
2. Discuss games with friends/bulletin boards	10
3. Comparative knowledge of the industry	10
4. Much more tolerant of frustration	9
5. Indications of early adoption behaviour	9
6. Desire to modify or extend games in a creative way	8
7. Technologically savvy	7
8. Have the latest high-end computers/consoles	7
9. Play for the exhilaration of defeating (or completing) the game	7
10. Hunger for gaming-related information	6
11. Engaged in competition with himself, the game, and other players	6
12. Willingness to pay	5
13. Prefer games that have depth and complexity	3
14. Time started playing games relative to the age of the industry	2
15. Prefer violent/action games	1

Game Experience Questionnaire – Core Module

Please indicate how you felt while playing the game for each of the items,
on the following scale:

not at all	slightly	moderately	fairly	extremely
0	1	2	3	4
< >	< >	< >	< >	< >

1. I felt content
2. I felt skilful
3. I was interested in the game's story
4. I thought it was fun
5. I was fully occupied with the game
6. I felt happy
7. It gave me a bad mood
8. I thought about other things
9. I found it tiresome
10. I felt competent
11. I thought it was hard
12. It was aesthetically pleasing
13. I forgot everything around me
14. I felt good
15. I was good at it
16. I felt bored
17. I felt successful
18. I felt imaginative
19. I felt that I could explore things
20. I enjoyed it
21. I was fast at reaching the game's targets
22. I felt annoyed
23. I felt pressured
24. I felt irritable
25. I lost track of time
26. I felt challenged
27. I found it impressive
28. I was deeply concentrated in the game
29. I felt frustrated
30. It felt like a rich experience
31. I lost connection with the outside world
32. I felt time pressure
33. I had to put a lot of effort into it

Appendix C

Consent Forms and Ethics Committee Approval

Consent Form for Participation in Research

Study Title: Brain-Computer Interface (BCI) assessment

Investigators: Athanasios Vourvopoulos (PhD Candidate)

Supervision: Dr. Sergi Bermudez I Badia

Purpose of this study

The purpose of this study is to evaluate user performance in a Motor Imagery Experiment using a Brain Computer Interfaces.

Procedures

You have been invited to participate in a neuroscientific experiment of the Neurorehab Lab research group of Madeira Interactive Technologies Institute. The session will take place in a research laboratory on the University of Madeira. For the experiment, three sessions of 1 hour (including equipment setup and instructions) in different days are required. For the procedure, first you are going to use a Brain Computer Interface (BCI), a non-invasive device to measure electric activity patterns of your brain. After verifying the connections, to be sure that the position of the electrodes of the BCI system are in the correct position, you will be given a set of instructions to carry out mental and physical. During these tasks we will record electroencephalographic (EEG) signals. You must try to execute the tasks as well as possible in the assigned period of time. In addition, in this experiment you will need to use a Head Mounted Display. Finally, a set of questionnaires will be supplied to be fill out each session. The experimental data will be processed in such a way that your anonymity will be preserved.

Participant Requirements-

You are eligible for participation if you: are 18-65 years old, are able to read, have no past of brain injuries and no neurological disorders.

Risks

The risk associated with participation in this study are no greater than those ordinarily encountered in daily life or during the performance of standard physical activity (e.g. simple muscular stretching). The EEG electrodes are superficial and DO NOT have any risk for your health. The interaction with the tasks requires executing repetitions (physical and mental) using a BCI on your head. You may experience fatigue and/or headache in some sessions.

Benefits

The study will contribute to the development of novel rehabilitation tools that in the future will help to patients with multiple neurological and motor disabilities.

Confidentiality

By participating in the study, you understand and agree that Neurorehab Lab may be required to disclose your consent form, data and other personally identifiable information as required by law, regulation, subpoena or court order. Otherwise, your confidentiality will be maintained in the following manner. Data and information gathered during this study may be used by Neurorehab Lab and published and/or disclosed by Neurorehab Lab to others of Neurorehab Lab for research purposes. However, your personal information will never be revealed in any publication or dissemination of the research data and/or results by Neurorehab Lab.

INFORMED CONSENT DOCUMENT

I understand that all information derived from the study **"Brain-Computer Interface (BCI) assessment"** is owned by the responsible research team. I give my consent for anonymous collection of data about me (results, pictures and videos), which will be stored and processed for scientific evaluation. I understand the significance of this information, and any questions I had were answered satisfactorily. I had enough time to decide on my participation in this study. I hereby consent my participation and the collection of information.

Signature of Participant Date

Signature of Investigator Date

Infor- conformidade
180627

(CES / SESARAM, EPE)

PARECER nº 15/2015

Sobre o Pedido/Estudo:
"Validação Clínica do Neurofeedback na Reabilitação Motora do AVC através de Imagiologia Cerebral"

A – RELATÓRIO

A.1 A Comissão de Ética para Saúde (CES) do Serviço de Saúde da Região Autónoma da Madeira, EPE (SESARAM, EPE), analisou o Documento Nº 25 na reunião de 11 de Maio de 2015, pedido de autorização do **Professor Sergi Bermúdez i Badia**, professor auxiliar da Universidade da Madeira, para a realização de projecto de investigação "**Validação Clínica do Neurofeedback na Reabilitação Motora do AVC através de Imagiologia Cerebral**". Trata de um estudo que pretende recolher informação sobre o efeito do uso de sistemas de Interface Cérebro Computador (ICC), como complemento da terapia convencional, em doentes que sofreram AVC.

A.2 O documento em análise é constituído por: oficio dirigido ao Conselho de Administração do SESARAM, EPE (E1573615) datado de 11 de Maio de 2015, que inclui questionário de submissão, projecto do estudo, documento de informação ao participante, parecer das direcções dos serviços de Medicina Física e Reabilitação e da Unidade de Neurorradiologia, termo de responsabilidade dos orientadores e curriculum vitae dos vários investigadores.
Acresce documento de consentimento informado recebido a 04 de Junho de 2015.

A.3 Trata-se de uma parceria entre o SESARAM e a Universidade da Madeira, cujo estudo tem por objectivo investigar áreas cerebrais activadas durante a imaginação cerebral e observação de tarefas implementadas através do paradigma ICC-RehabNet, sistema baseado na realidade virtual utilizado na reabilitação dos défices motores dos membros superiores após lesão cerebral. Pretende ainda quantificar a extensão da neuroplasticidade induzida pelo paradigma ICC-

RehabNet comparando uma avaliação pré e pós intervenção com a duração de 1 mês. Serão recrutados 20 doentes com défices pós-AVC (10 intervenção mais 10 controlo) que no âmbito dos tratamentos de reabilitação habitual, que serão distribuídos de forma aleatória os grupos, sendo o grupo de intervenção aquele que fará o tratamento com ICC.

B – IDENTIFICAÇÃO DAS QUESTÕES COM EVENTUAIS IMPLICAÇÕES ÉTICAS

B.1 Serão salvaguardados, ao longo de todas as fases do estudo, os princípios éticos relativos aos estudos de investigação, nomeadamente no que se refere ao anonimato dos participantes e confidencialidade dos dados.

B.2 Reconhece-se a pertinência do estudo e o interesse prático nos resultados esperados, sendo que a metodologia utilizada salvaguarda os direitos dos participantes.

C – CONCLUSÂO

A CES/SESARAM, EPE deliberou emitir **Parecer Favorável,** condicionado à apresentação dos documentos em falta.

À data da assinatura deste parecer esta situação já se encontrava regularizado (conforme mencionado em A.2.).

O presente estudo foi assim aceite por não se colocarem quaisquer questões de ordem ética.

Aprovado em reunião dia 11 de Maio de 2015, por unanimidade.

Funchal, 19 de Junho de 2015.

O Presidente da CES/SESARAM, EPE

Santos

(Ricardo Santos)

SERVIÇO DE SAÚDE DA REGIÃO AUTÓNOMA DA MADEIRA, E.P.E.
Hospital Central do Funchal
Serviço de imagiologia

Nome: [redacted] Pr.Cl.: RAM-[redacted]
Exame: [redacted]
Local: Imagiologia-Nélio Mendonça Data: [redacted] Hora: ~~11:30~~

Ressonância Magnética

INFORMAÇÃO E PREPARAÇÃO:

Não podem realizar este exame as pessoas com PACEMAKER cardíaco ("pilha no coração"),

Se já foi operado a artérias ou ao cérebro e tem "clips" metálicos também não pode realizar este exame. Implantes cocleares, expansores de tecidos, próteses oculares, implantes dentários, neuroestimuladores, estimuladores do crescimento ósseo, desfibrilhadores cardíacos implantáveis, bombas de perfusão de drogas implantáveis, também condicionam a realização do exame.

Outros objectos metálicos ferromagnéticos podem sofrer efeitos de aquecimento, artefacto e podem mesmo sofrer algum grau de deslocamento. Dentro destes, incluem-se alguns tipos de "clips" vasculares intracraninanos, guias, filtros e stents intravasculares (sobretudo nas primeiras semanas após a sua colocação), clips vasculares extracranianos (nas primeiras 4-6 semanas, reavaliando cada caso isoladamente), válvulas de acesso vascular, válvulas cardíacas, corpos estranhos intra-oculares, balas, projécteis e estilhaços, implantes e próteses ortopédicas.

É muito importante que avise o seu médico assistente, assim como o médico radiologista, o enfermeiro ou o técnico de radiologia, antes da realização do exame.

RECOMENDAÇÕES GERAIS:

Deve trazer sempre todos os exames anteriores.

À chegada ao Serviço de Imagiologia deve informar-nos se é diabético insulino-dependente.

O exame poderá não ser feito por ordem de chegada, uma vez que poderá haver exames de urgência.

Este exame é contra-indicado em doentes portadores de aparelhos que possam ser activados eléctrica ou magneticamente. Os aparelhos contra-indicados são: pacemaker cardíaco ("pilha no coração"), implantes cocleares, expansores de tecidos, próteses oculares, implantes dentários, neuroestimuladores, estimuladores do crescimento ósseo, desfibrilhadores cardíacos implantáveis, bombas de perfusão de drogas implantáveis.

Outros objectos metálicos ferromagnéticos podem sofrer efeitos de aquecimento ou artefacto e podem mesmo sofrer algum grau de deslocamento. Dentro destes, incluem-se alguns tipos de "clips" vasculares intracraninanos, guias, filtros e stents intravasculares (sobretudo nas primeiras semanas após a sua colocação), clips vasculares extracranianos (nas primeiras 4-6 semanas, reavaliando cada caso isoladamente), válvulas de acesso vascular, válvulas cardíacas, corpos estranhos intra-oculares, balas, projécteis e estilhaços, implantes e próteses ortopédicas.

~~Em caso de claustrofia pode ser necessário recorrer a sedação ou anestesia para realizar o exame.~~

Serviço de Imagiologia - Hospital Dr. Nélio Mendonça
Av Luís de Camões 9004 – 514 Funchal
Fax 291 753 274 – secradiologia@srs.pt

SESARAM

SERVIÇO DE SAÚDE DA REGIÃO AUTÓNOMA DA MADEIRA, E.P.E.
Hospital Central do Funchal
Serviço de imagiologia

	Sim	Não		Sim	Não
Se mulher em idade fértil, está grávida?	☐	☐	Insuficiência Renal	☐	☐
Pacemaker	☐	☐	Tatuagens	☐	☐
Clips cirúrgicos	☐	☐	Balas, chumbos,esquírulas metálicas	☐	☐
Válvulas derivação	☐	☐	Clips Aneurismas	☐	☐
Suturas metálicas	☐	☐	Próteses cardíacas metálicas	☐	☐
Estimuladores de Crescimento	☐	☐	Próteses Ortopédicas	☐	☐
Neuroestimuladores	☐	☐	Próteses auditivas	☐	☐
Cateteres	☐	☐	Próteses oculares	☐	☐
Dispositivos Intra-uterinos	☐	☐	Próteses dentárias fixas	☐	☐
Filtros vasculares	☐	☐	Claustrofobia	☐	☐

Consentimento dado por ☐ Doente ☐ Pais ☐ Representante Legal

Declaro que:

me considero informado acerca do exame imagiológico que me foi proposto, e que autorizo a realização do acto médico descrito, bem como os procedimentos adicionais decorrentes daqueles actos e que possam vir a ser necessários no meu próprio interesse, justificados por razões clínicas;

tive a oportunidade de fazer perguntas, que me foram respondidas. Compreendo que posso retirar este consentimento em qualquer altura antes da realização do procedimento;

(se mulher em idade fértil) não estou nem suspeito estar grávida.

Pelo doente: Assinatura do doente: ..../...../20.....

Estando o doente incapacitado:

Assinatura do ☐ Pai/Mãe ☐ Filho(a) ☐ Cônjuge ☐ Tutor ☐ Outro

Nome: ..../...../20....

BI: .... de ...../...../........ Arquivo de identificação..

Morada..

Grau de Parentesco ....

Pelo médico:

Confirmo que foram explicados ao ☐ Doente ☐ Pais ☐ Representante Legal, de forma adequada e inteligível o exame imagiológico a efectuar, assim como os riscos complicações, e as alternativas possíveis à situação clínica. Todas as questões foram respondidas e o doente concordou com o plano.

Nome clínico e nº mecanográfico ....

Data ...../...../2......

Se tiver alguma dúvida contacte-nos para o Serviço Central (Hospital Dr. Nélio Mendonça), das 11 às 12h, pelo telefone 291 705600 ou para o Hospital dos Marmeleiros, pelo telefone 291 705300.