UNIVERSIDADE da MADEIRA

INTEGRATING EYE TRACKING IN VIRTUAL REALITY FOR STROKE REHABILITATION

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ABSTRACT

This thesis reports on research done for the integration of eye tracking technology into virtual reality environments, with the goal of using it in rehabilitation of patients suffering from stroke.

For the last few years, eye tracking has been a focus on medical research, used as an assistive tool – to help people with disabilities interact with new technologies – and as an assessment tool – to track the eye gaze during computer interactions. However, tracking more complex gaze behaviors and relating them to motor deficits in people with disabilities is an area that has not been fully explored, therefore it became the focal point of this research.

During the research, two exploratory studies were performed in which eye tracking technology was integrated in the context of a newly created virtual reality task to assess the impact of stroke. Using an eye tracking device and a custom virtual task, the developed system is able to monitor the eye gaze pattern changes over time in patients with stroke, as well as allowing their eye gaze to function as an input for the task.

Based on neuroscientific hypotheses of upper limb motor control, the studies aimed at verifying the differences in gaze patterns during the observation and execution of the virtual goal-oriented task in stroke patients (N=10), and also to assess normal gaze behavior in healthy participants (N=20). Results were found consistent and supported the hypotheses formulated, showing that eye gaze could be used as a valid assessment tool on these patients. However, the findings of this first exploratory approach are limited in order to fully understand the effect of stroke on eye gaze behavior.

Therefore, two novel model-driven paradigms are proposed to further understand the relation between the neuronal mechanisms underlying goal-oriented actions and eye gaze behavior.

KEYWORDS: Eye tracking; gaze behavior; virtual reality; stroke; rehabilitation.

RESUMO

Esta tese descreve a investigação realizada para a integração de tecnologia de *eye tracking* em ambientes de realidade virtual, com o objectivo de utilizá-la na reabilitação de pacientes que sofreram acidente vascular cerebral (AVC).

Nos últimos anos, o rastreamento ocular tem sido um foco na investigação médica, sendo usado como ferramenta de apoio – para ajudar pessoas com deficiência a interagir com novas tecnologias – e como ferramenta de avaliação – no rastreamento do olhar durante interações com computador. No entanto, fazer o rastreamento de comportamentos do olhar mais complexos e relacioná-los com défices motores em pessoas incapacitadas, é uma área que ainda não foi totalmente explorada e, por isso, tornou-se o ponto focal desta investigação.

Durante a investigação, dois estudos exploratórios foram realizados onde tecnologia de *eye tracking* foi integrada com uma tarefa de realidade virtual, para avaliar o impacto do AVC em pacientes. Usando um dispositivo de *eye tracking* e um ambiente virtual, foi desenvolvido um sistema capaz de monitorizar as mudanças nos padrões do olhar ao longo do tempo em pacientes, bem como de permitir a utilização do olhar para a interacção com o sistema.

Com base em hipóteses neurocientíficas de controlo motor, os estudos tiveram como objectivo verificar as diferenças nos padrões do olhar durante a observação e execução de uma tarefa virtual em pacientes de AVC (N=10), assim como avaliar o comportamento normal do olhar em participantes saudáveis (N=20). Os resultados encontrados foram consistentes e apoiaram as hipóteses formuladas, mostrando que o olhar pode ser usado como uma ferramenta de avaliação válida neste tipo de pacientes. No entanto, as conclusões desta abordagem exploratória mostrou-se limitada para compreender plenamente os efeitos do AVC no comportamento do olhar.

Portanto, são propostos dois novos paradigmas baseados em modelos, de modo a entender melhor a relação entre os mecanismos neuronais, subjacentes às acções orientadas a objectivos, e o comportamento do olhar.

PALAVRAS-CHAVE: Rastreio ocular; comportamento do olhar; realidade virtual; AVC; reabilitação.

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1. INTRODUCTION

1.1 MOTIVATION

Neurological disorders, such as stroke, are a leading cause of permanent disability among the current population, and are considered by the World Health Organization as one of the greatest threats to public health [1]. Since most patients with these injuries will survive the initial illness, the greatest health effect is usually caused by the long-term consequences for the patients and their families. As a result, neurorehabilitation has been essential to aid patients recover from such neurological injuries, and minimize/compensate for any functional change that may result from them.

Neurorehabilitation involves many areas of study and focuses on therapies that help people live their everyday lives, thus improving their quality of life. The therapies range from motor rehabilitation that aims at regaining motor functions, to cognitive rehabilitation that treats deficits related to attention, memory, visuospatial skills, and executive function. While most motor rehabilitation therapies are based on stimulating the affected limb to induce neuroplasticity, recent approaches based in action observation have been proven to also have a positive effect on the recovery process. The reasoning behind this is the existence of mirror neurons – areas of the brain that are activated both during the execution of an action and during the observation of that same action – which open up new possibilities for the treatment of neurological deficits.

Over the last decade, researchers have been combining science and technology to develop several new therapy methods for rehabilitation. These include the use of video games and virtual reality (VR), which offer potential for motivating patients to perform specific tasks that traditional therapies do not provide, as well as allowing for a more controlled rehabilitation environment. Eye tracking is another technology used in research to acquire a better understanding of neurological functions, and related disorders and impairments. For instance, investigating gaze patterns and control mechanisms of eye movements can provide early indicators for certain neurological disorders, while being more accessible, unobtrusive and affordable than other assessment tools.

With these new methods, automated assessment processes and the ability to quantify data provide new therapeutic opportunities that make it possible to follow the rehabilitation process in an objective and quantifiable way. Thus, many clinics and hospitals are adopting these solutions for social interaction, training and rehabilitation since they are affordable, accessible and can be used both in the hospital and at the patients' home. In the future, with the ever-increasing inclusion and ubiquity of new technologies in our lives, it is expected that neurorehabilitation therapies will follow this path, making the integration of such technologies in rehabilitation an important and challenging step of this process.

1.2 OBJECTIVES

The main objective of this thesis is to research novel methods of assessment and rehabilitation in patients suffering from neurological deficits, by developing a system that integrates eye tracking technology into virtual reality environments. However, the thesis does not only cover the technical implementation process of the system, but mainly focuses on the research done with it and its results in a rehabilitation context.

The goal of the research is to go beyond the current state of the art and propose a novel system with potential to be used as a diagnostic and rehabilitative tool for post-stroke patients. In terms of technology, the software should integrate virtual environments built with the Unity game engine (Unity Technologies, San Francisco, USA), with a Tobii Eye Tracker (Tobii Technology, Stockholm, Sweden) as the eye tracking device. The final system would be able to monitor the eye gaze changes of the user over time, and thus could serve as a tool to assess gaze movements and also as an input method. For the proof of concept, the system would have to be validated in experimental studies with healthy users, but also with stroke patients in a hospital environment. From this validation, and based on the results found, a new paradigm to evaluate and rehabilitate deficits in post-stroke patients would be proposed.

1.3 DOCUMENT STRUCTURE

This document is organized into seven chapters, having the following structure. In chapter 1, the context and motivation for the thesis are introduced, as well as the focal objectives of the research and the overall document organization. Chapter 2 presents a literature review of stroke rehabilitation, focusing on new neurorehabilitation techniques to treat motor deficits in stroke patients. More so, it presents novel approaches that use technology for rehabilitation purposes. It concludes with the direction taken from the literature review, connecting it to the research objectives of the thesis. In chapter 3, the system developed for the research is described, explaining the approach used for the integration of eye tracking and virtual reality, and its detailed implementation in terms of hardware and software. In chapter 4, the first of two exploratory studies conducted with the system is presented. A study with stroke patients is described, presenting its findings and conclusions. In chapter 5, the second study performed with the system is presented. A study conducted with healthy participants is described, presenting its findings, conclusions and connection to the first study. Chapter 6 presents a new model-driven rehabilitation paradigm that resulted from the findings of the research activities, and connects it to future work perspectives. Finally, chapter 7 finishes with the discussion and main conclusions taken from the research developed.

2. STATE OF THE ART

This chapter includes the literature review of the main topic of the thesis, which aims at giving a better understanding of the current methods and approaches involved in stroke rehabilitation. It starts by presenting an overview of the current state of stroke and techniques used in neurorehabilitation, and then focuses on the role of the mirror neurons as a new concept in the recovery of the patients. It continues by highlighting some novel technological approaches that use virtual reality and eye tracking for assessment and rehabilitation purposes. The chapter concludes with the direction taken for the research from the current state of the art.

2.1 STROKE REHABILITATION

Stroke is a global healthcare problem that is frequent, severe, and disabling. In most countries, stroke is the second or third most common cause of death and one of the main causes of permanent disability in the adult population [2]. Although remarkable improvements have been made in the management of stroke, without a widely applicable and effective medical treatment most post-stroke care will continue to rely on rehabilitation interventions [3].

The long-term effect of stroke is determined by the location and size of the brain lesion and by the extent of its recovery. This recovery is a complex process that probably occurs through a combination of natural and learning-dependent processes, including restoring the functionality of affected neural areas, reorganization of neural circuitry to relearn lost motor and cognitive functions, and improvement of the discrepancy between the impairment of a patient and the demands of their environment [4]. Although patient results and individual recovery patterns vary, several studies suggest that recovery of motor functions and activities is predictable in the first days after stroke [4, 5], and that long-term survival can be predicted by functional outcome after six months [6].

The traditional neurorehabilitation approaches for the treatment of motor deficits in stroke patients are mostly based on techniques with the goal of stimulating the use of the paretic arm during training sessions. The main principle is that repetitive active movements of an affected limb leads to effects induced by positive neuronal plasticity. The effects of this repetitive training are experimentally well proven [7, 8, 9, 10], and this approach was demonstrated to be more effective than physiotherapeutic techniques, showing smaller learning time of arm movements, shorter therapy duration and faster recovery.

Examples of these conventional approaches include: constraint-induced movement therapy [11] - that combines restraint of the unaffected limb and intensive use of the affected limb; motor relearning [12] - task-oriented functional training; and repetitive arm training [13]. However, these more traditional neurorehabilitation techniques do not directly consider the brain mechanisms for recovery, and as such new and more efficient methods could be developed, based on the current scientific knowledge, to complement and improve the rehabilitation process.

2.2 MIRROR NEURONS

There has been increasing experimental evidence that motor areas are recruited not only when movement actions are executed, but also when they are mentally rehearsed – motor imagery – or merely observed – action observation [14]. The neurophysiological basis for this recruitment relies on the discovery of mirror neurons, first reported in monkeys [15]. These mirror neurons discharge when the subject performs an object-related action with the hand and when it observes the same or a similar action done by another individual. In humans, it has also been shown that action observation recruits the same motor representations active during the actual execution of those same actions [16, 17].

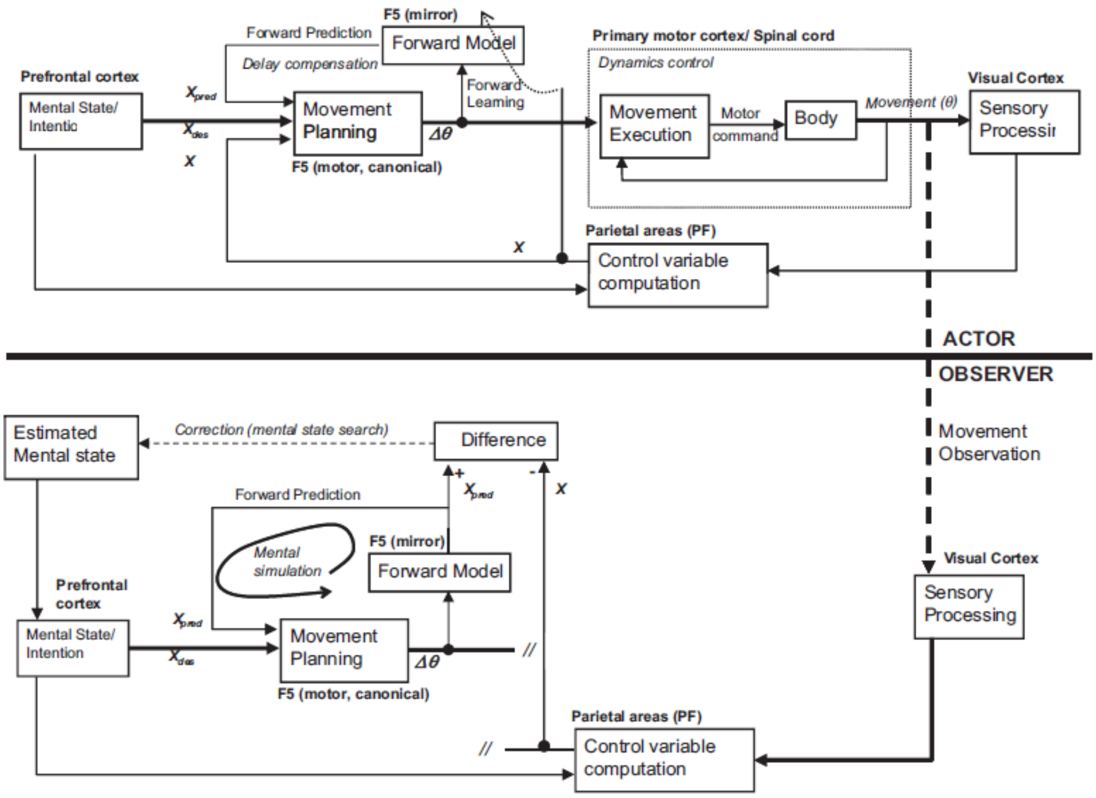

FIGURE 1 - The Mental State Inference model adapted from Oztop, et al. **[18]**.

In [18], Oztop, et al. present the Mental State Inference model (see Figure 1) to explain how an observer can obtain an estimate of the executor's goal or intention based on visual observation. According to this model, the dual activation of mirror neurons is explained by the two following processes: i) automatic engagement of Mental State Inference during action observation, and ii) forward prediction task undertaken by the mirror neurons for motor control during action execution.

From a rehabilitation point-of-view, some studies [19, 20] showed strong evidence that motor imagery and action observation have a positive effect on rehabilitation of motor deficits after stroke, reporting that this effect appears to be superior to traditional programs and that action observation is leading to a significantly higher impact on recovery than physical training alone. However, this should not be seen as replacement for physical exercise but rather as a complementary, yet relevant, technique to improve motor rehabilitation.

Through neuroimaging techniques, such as functional magnetic resonance imaging (fMRI), researchers were able to locate specific areas of brain activation and highlight the spatial and temporal congruency between observing, executing, and imaging object-related actions. There is now a common understanding that the covert elements (attention, motor planning) of action execution, action observation and motor imagery share, at least in part, similar neural networks and mechanisms [21, 22], reinforcing the role played by the mirror neurons in these neural mechanisms.

In addition to neurological analysis techniques, one promising method of quantifying imagery and observation of goal-directed action is by measuring eye movements [23, 24], which may provide an online indication of some of the attentional and cognitive processes [25] that occur during such actions. Furthermore, during motor planning, gaze performs an active role in action observation linked to sensory prediction, just as it does during an execution [26].

2.3 Eye Tracking as Assistive Technology

For several years, eye tracking technology has been used in medical research. Since the early 1970s there has been notable development in eye tracking systems related to the evolution of marketing and design. With this growing development, new methodologies for research application, mainly in HCI [27], have been possible. Thanks to its flexibility to adapt to different contexts of use, the eye tracker is considered as a promising technology able to overcome or decrease the difficulties which arise during the access to technology, namely as an assistive technology, for people with disabilities.

Since the 1980s, the focus of HCI has been directed toward the use of eye tracking technology as an input device [28, 29] with the specific intent to facilitate communication and control for people with disabilities, such as people with stroke. In [30], Jacob claims that the use of eye tracker as an input device raises two main issues. The first one is connected to the ocular system function, which is primarily used as a sensory channel of visual input rather than as a motor system of communicative activity, which can cause what the author refers to as the "Midas Touch problem" - the over-activation of the system in response to every single eye movement [30]. The second issue raised concerns both the accuracy of the eye tracking techniques, which is closely related to the precision of calibration, and the accuracy of the interactive areas of the interface, which are often too large compared to the perceptual capacity of the foveal region [31]. This issue, however, has been partially solved with the increasing accuracy of most recent eye trackers.

Recently, researchers have paid more attention to the interactive components of the system by either proposing design solutions or carrying out usability evaluations on some current systems. In [32], Porta and Ravelli attempted to overcome the accessibility problems arising for people with motor disabilities, by developing an entirely eye-based browser, which combines eye scrolling and selection techniques to provide web browsing by means of eye movements. Eye-tracking techniques have also been applied to the study of the remote control of environment through different assistive technologies, for instance eye-controlled wheelchairs designed for people with cerebral palsy [33] and eye-control devices based on electrooculography [34, 35], which are significantly less invasive than most common technologies based on EEG or BCI.

2.4 Novel Approaches to Neurorehabilitation

In the last few years, several studies have been trying to demonstrate the feasibility of systems that incorporate virtual reality and/or eye tracking into neurorehabilitation. The next sections present a short review of the most relevant works to this research.

2.4.1 Training Virtual Street-crossing in Stroke Patients

In [36], Navarro, et al. describe the design and validation of a low-cost virtual reality system for training street-crossing in stroke patients with and without unilateral neglect, using healthy subjects as a control group.

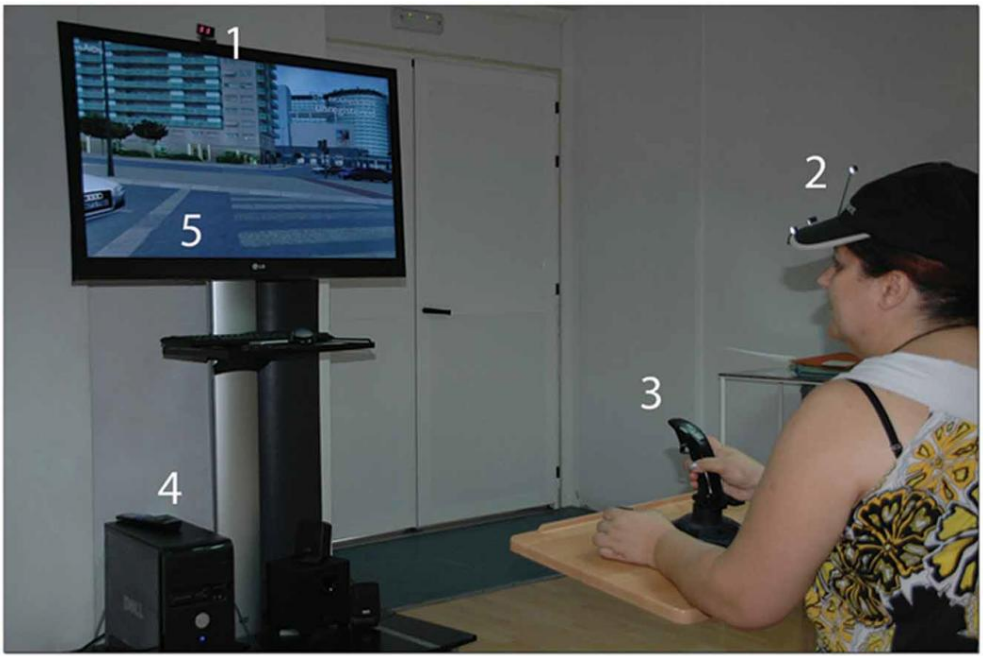

Figure 2 - VR street-crossing system setup used by Navarro, et al. **[36]**.

As can be seen in Figure 2, the virtual reality street-crossing system consisted of a TrackIR 4:PRO head tracking system (NaturalPoint, Corvallis, USA; 1 and 2), a joystick (3), a standard PC (4) and a 47" LCD screen (5). Participants' interaction was defined by their head rotations, estimated by the infrared camera from the orientation of the constellation of reflective marks, and by their displacement in the virtual environment estimated by the joystick. The virtual environment recreated a real street intersection in the city of Valencia, and the virtual world is presented using a first-person view. In each session, the participants were asked to move from the starting point to a large department store and then to come back as quickly and safely as possible. In addition to the VR results and questionnaire, the stroke participants were assessed with a series of neuropsychological tests by an expert therapist.

The results showed that participants from the control group completed the task more quickly and safely than the participants from the experimental group, and in turn, the participants from the experimental group without neglect finished the task more quickly and safely than the participants with neglect. Stroke patients had more difficulty crossing the street safely than healthy controls. Patients with neglect demonstrated a dramatic lack of efficacy. The authors concluded that the VR system was potentially both entertaining and motivating, as reflected by the scores from the questionnaire.

Despite not involving full tracking of eye movements (only tracking of head movements), this study demonstrates the validity of using VR in conjunction with a tracking system to gather information about gaze. A system like this one could be used as an assessment and training tool, while keeping high levels of motivation and entertainment in the participants.

2.4.2 Eye-Controlled System for Children with Cerebral Palsy

In [37], Amantis, et al. present a study to understand if eye tracking technologies could be considered as a valid tool for rehabilitation of children and adolescents with cerebral palsy. Participants consisted of an experimental group with children suffering from cerebral palsy and a control group with children with no disabilities.

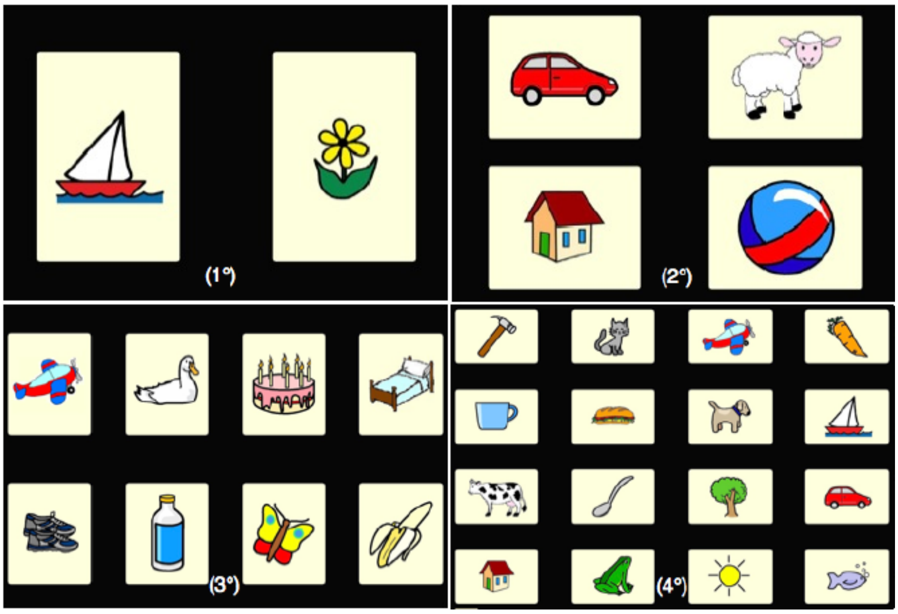

Figure 3 - Layout of the eye-pointing grids used in the system for children with cerebral palsy by Amantis, et al. **[37]**.

The system was composed of a portable 15" MyTobii P10 (Tobii Technology, Stockholm, Sweden) and a laptop to record the sessions. During each session, four grids composed by multiple icons were presented (see Figure 3), so participants could identify and select with their eye gaze the given target icon.

The authors concluded that, compared to the control group, the experimental group's performance had a significant difference in terms of efficiency, showing both higher completion times and errors. However, the authors recommended that further developments with a larger number of participants were necessary to investigate more deeply the effectiveness of the current eye tracking system.

This study shows that using eye gaze as a form of input may be viable option for training and rehabilitating children with cerebral palsy, which suggests that a similar experimental setup could be used with post-stroke patients.

2.4.3 INTEGRATED ELECTROMYOGRAM AND EYE GAZE TRACKING CURSOR CONTROL SYSTEM

In [38], Chin, et al. present the implementation and testing of an integrated electromyogram (EMG) and eye gaze tracking (EGT) system for patients with motor disabilities. The EMG subsystem consisted of several electrodes, placed on the face of the user; while the EGT subsystem was an R6-HS eye tracking system (Applied Science Laboratories, Bedford, USA). Two experiments were conducted to compare the integrated system with an EGT-only system.

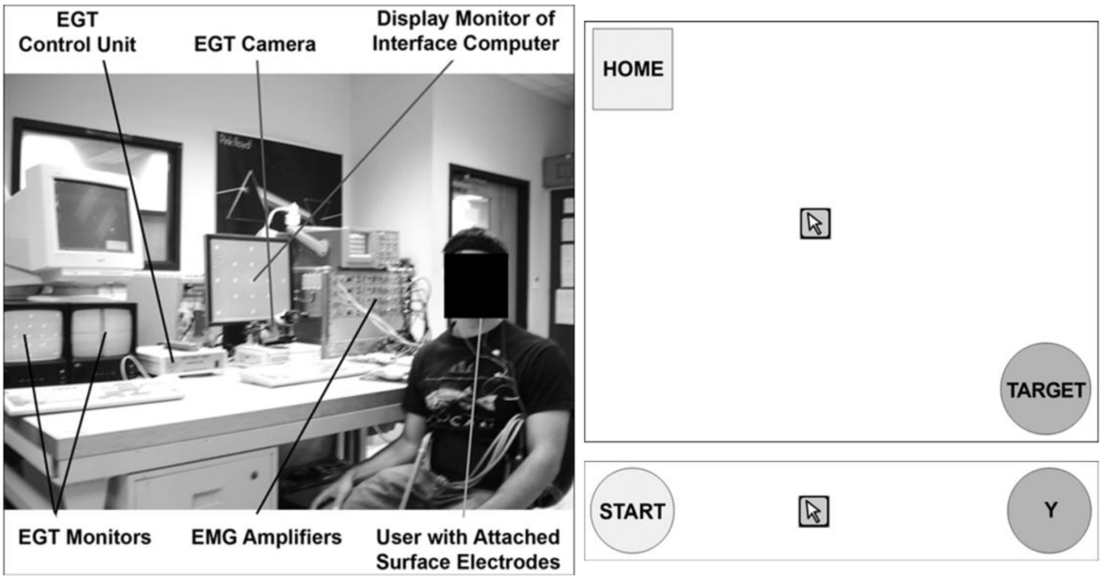

FIGURE 4 - Setup and layout of the EMG/EGT system used by Chin, et al. **[38]**. Left, EMG/EGT system components, including experimental instruments. Right, point-and-click trial layout for experiment 1 (top) and experiment 2 (bottom).

For the first experiment, the authors wanted to test whether the EMG/EGT-based input would produce lower error rates and comparable task times with those recorded for EGT-only and mouse input. Each layout contained a square icon labeled "HOME" and a circular icon labeled "TARGET" (see FIGURE 4, top-right). The subjects were instructed to click the "HOME" icon, move the cursor to the "TARGET" icon, and then click the "TARGET" icon. Results revealed that the EMG/EGT technique was significantly slower than both the mouse and EGT. They also revealed that the EMG/EGT technique had a significantly smaller error rate than the EGT technique, and was comparable with that of the mouse.

For the second experiment, authors tested whether the EMG/EGT-based input could produce a lower error rate than the EGT-based input when the source of error was exclusively due to unintended gaze-based selections. To test this, they used only large icons, to minimize errors associated with EGT accuracy limitations. Each trial displayed a green circle labeled "START" separated from a red target circle labeled "Y" or "N" (see FIGURE 4, bottom-right). The objective was to have the user select the "START" circle and then move the cursor toward the target circle. The user must then select the target only if a "Y" label was displayed within it but not if an "N" label was displayed. Results showed that the mean error rate was lower for the EMG/EGT technique compared with the EGT technique.

The authors concluded that the EMG/EGT system was a viable option for providing individuals with motor disabilities access to computers. The EMG/EGT technique was not as fast as EGT

but provides increased reliability. Authors also stated that further improvements in usability and accessibility were required and user testing with individuals with motor disabilities was to be continued.

While not having tested the system with actual people with disabilities, these two experiments show the viability of combining eye tracking technology with EMG as a means of interacting with computers. However, results indicate that the EMG/EGT technique is not as fast and, in some cases, people with motor disabilities may not be able to even profit from the EMG interaction, which can arguably make it worse than standard eye tracking techniques.

2.4.4 Gaze Tracking Guidance for Upper Limb Robot-Aided Neurorehabilitation

In [39], Loconsole, et al. propose a new gaze based control system to provide active guidance to the upper limb movement, through a robotic arm.

The Hybrid Bionic System presented was composed of four components: the L-EXOS - allows the user's right arm to move, in both passive and semi-active mode, with the purpose of accomplishing reaching tasks; the eye tracker - determines the user's gaze direction in real world; the scene camera - used in association with eye tracking to select the target the user is looking at; and the environment camera - locates the target in 3D space and communicates the target position to the L-EXOS controller.

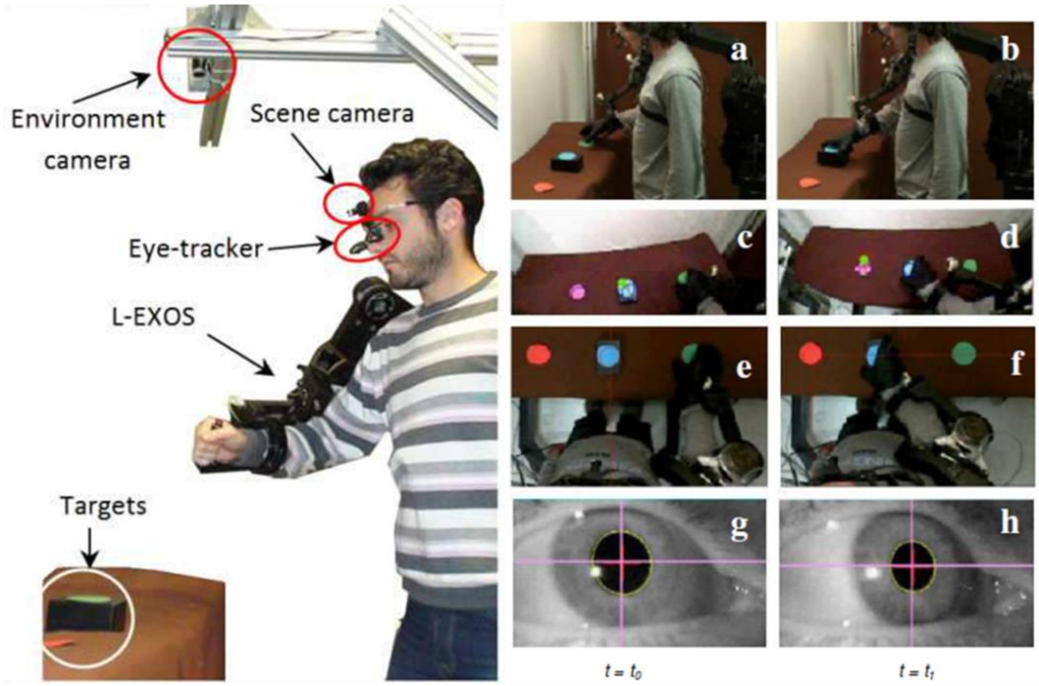

Figure 5 - Hybrid Bionic System used by Loconsole, et al. **[39]**. Left, complete system setup. Right, state of the experiment at time t0 and t1 from the different points-of-view: external camera (a, b), scene camera (c, d), environment camera (e, f) and eye tracker infrared camera (g, h).

For the study, one healthy subject was asked to perform a simple manual task consisting in reaching a box and then grasp and move it to another location. The subject was asked to keep the arm passive and let it be moved by the L-EXOS. The selection of the target to be moved was performed by watching the desired target.

The authors concluded that the experimental results demonstrated the feasibility of the proposed system and the novelty the system introduces in the field of eye-based rehabilitation systems. For future work, authors suggested that the proposed method should be extended with the recognition of real objects and not only colored targets. Authors also stated that a clinical evaluation of the proposed rehabilitation training was on-going in a group of post-stroke patients.

Despite not providing a virtual environment for the task, this study shows that the combination of eye tracking with an assistive robotic arm is possible in a rehabilitation context, especially if used in a reach-and-grab task. This concept could easily be translated to a virtual environment, where eye movements would serve as assessment metrics for the task.

2.5 Conclusions

From a stroke recovery standpoint, conventional rehabilitative techniques do not directly take into consideration brain mechanisms for recovery and seem to have reached their best possible outcomes. Therefore new approaches are needed to continue to improve the current rehabilitation process. Based on the concept of mirror neurons, researchers have reported evidence that motor imagery and action observation have a positive effect on rehabilitation of motor deficits, showing a significantly higher impact than traditional neurorehabilitative programs alone. This is a clear indication that new research methodologies for stroke rehabilitation need to follow this direction, and explore the concepts of motor imagery and action observation as a rehabilitative tool.

From a technological perspective, the use of eye tracking tools has been growing over the last decades in medical research, mainly as an assistive technology, by allowing people with motor disabilities to have access to information technologies. In most recent years, however, there have been several attempts to look at new approaches that incorporate eye tracking with virtual reality and even robotics with the goal of improving on the conventional rehabilitation methods. These new approaches show promising results, which demonstrate the feasibility of using eye tracking in a rehabilitation context and that more studies need to be conducted to better understand the potential of this technology.

The review presented shows that eye tracking is a powerful technology that can be used in conjunction with other tools. However, despite the significant developments in stroke rehabilitation and eye tracking, there is still a lack of work in the area of research that combines both, in particular to use eye movements as a means of assessing the impact of stroke. As a result, this thesis proposes the use of eye tracking technology as a valid tool for assessment and rehabilitation of post-stroke patients. Furthermore, the combination of eye tracking with virtual reality would be essential to allow a more controlled and customized environment, which in turn would make it more entertaining and engaging for the patients.

3. SYSTEM OVERVIEW

This chapter describes the virtual reality-eye tracking (VR-ET) system developed for this research by discussing the paradigm behind it and its implementation. The chapter starts by introducing the general approach used for the creation of the system, and then continues with a detailed description of the hardware and software used for its development. The chapter ends with the implementation and the resulting system that would ultimately be used in an experimental environment.

3.1 NOVEL VR-ET TRAINING APPROACH

Several VR systems have been proposed for the recovery of motor deficits following stroke. Most of them adopt the traditional approach of repetitive active movement of the affected limb, and translate conventional rehabilitative tasks to a virtual environment. Since this approach is not based on neuroscientific models of recovery and has the limitation that only patients with active movement capabilities can profit from, there is a need for a new paradigm that can complement and improve it. In order to address these limitations, the VR-ET approach aims at exploring the potential of using eye gaze movements during observation and execution of goal-oriented tasks in a virtual environment for assessment and rehabilitation purposes.

On the one hand, recording eye gaze during such tasks can give valuable information on the eye movements generated, which provide an indication of the attentional and cognitive processes behind it. On the other hand, eye gaze can be used as a direct input mechanism for task execution, by mapping the eye gaze movements recorded back to the virtual environment. From a rehabilitation point of view, the VR-ET approach intends to use a rehabilitative method based in action observation and execution, exploiting the concept of mirror neurons. Since these neurons support both execution and observation, motor areas may possibly be stimulated and rehabilitated, to some extent, by mere observation of stimuli associated with motor actions. The eye gaze movements recorded can be used to quantify the observation and execution of the goal-oriented actions in a meaningful manner, providing an automated and objective way to assess the impact of stroke in patients.

To implement the VR-ET approach, and based on previously reviewed studies that use eye tracking in goal-oriented tasks [23, 26, 39], a simple reach-grab-release virtual task was designed (see section *3.3.3.2 Virtual Task Module* for more details) to be used in a rehabilitation context. The task offers three conditions: observation, arm-controlled execution, and eye-controlled execution. During the task, stroke patients observe/execute reaching and grasping actions with both their paretic and non-paretic arm, while their eye gaze is recorded and analyzed. Under the assumption of interference between the neuronal circuits underlying execution and observation, it is expected to detect some differences in the gaze metrics between observation/execution with paretic vs. non-paretic arm across the three conditions. These results can then be used for diagnostic and rehabilitation of the patients.

By directly taking into account the neural mechanisms involved in the recovery process, which in this case are measured through the eye movements, it is expected that this training approach will be more efficient and provide a higher impact than conventional techniques.

3.2 HARDWARE

In terms of hardware, the eye tracking device used for the acquisition of the eye gaze data was the Tobii T120 Eye Tracker (see Figure 6). This eye tracker is integrated in a monitor and is designed for all types of eye tracking studies where the stimuli can be presented on the display, making it ideal for the research approach taken.

FIGURE 6 - Tobii T120 Eye Tracker - easy to use, unobtrusive, and allows free and natural head movements.

Accuracy	~ 0.5 degrees
Data rate	60 or 120 Hz
Freedom of head movement	30x22x30 cm
Display	17" TFT, 1024x768 pixels
Weight	~ 9 kg

TABLE 1 - Technical specifications of the Tobii T120 Eye Tracker.

The device can be set up easily, providing a highly portable solution, which was required since the development and deployment of the system would occur in separate locations. The eye tracker provides high accuracy and allows for a large degree of head movement (see Table 1), permitting users to move freely, ensuring natural behavior and therefore valid results for the research.

The Tobii T120 Eye Tracker is also supported by the Tobii SDK, which offers a comprehensive set of tools for the implementation of the VR-ET system. The SDK provides access to the gaze data (detailed below), setting of the calibration for finer integration of SDK applications and the eye tracker, and complete documentation for the supported languages (C++, C#, Python and MATLAB).

The SDK API makes it possible to subscribe to a data stream that will arrive to the client application according to the eye tracker sampling frequency. Here is a summary of the data included in each sample.

- **Time Stamp:** Time when a specific gaze data sample was sampled by the eye tracker.
- **Eye Position:** The eye position is provided for the left and right eye individually and describes the position of the eyeball in 3D space, in the UCS coordinate system.
- **Relative Eye Position:** The relative eye position is provided for the left and right eye individually and gives the relative position of the eyeball in the head box volume as three normalized coordinates.
- **Gaze Point:** The gaze point is provided for the left and right eye individually and describes the position of the intersection between the line originating from the eye position point with the same direction as the gaze vector and the calibration plane (see Figure 7). The gaze vector can be computed by subtracting the 3D gaze point and the 3D eye position and normalizing the resulting vector.

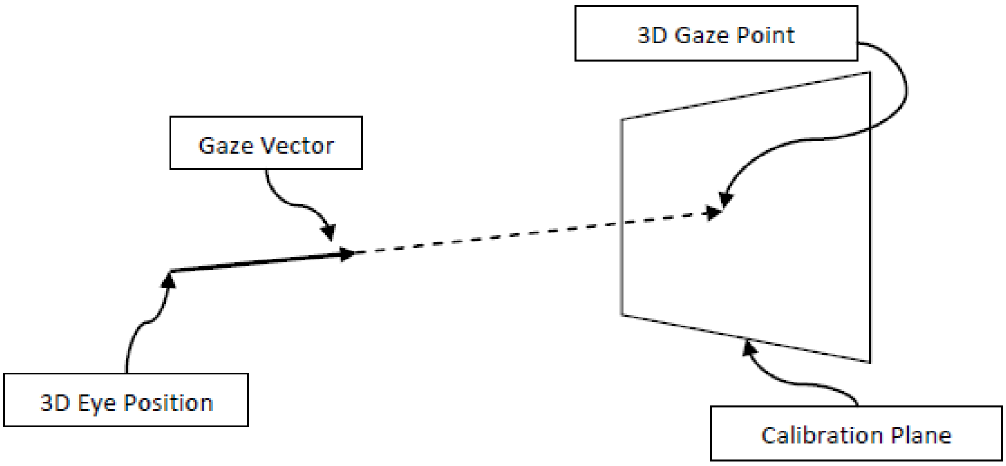

FIGURE 7 - Gaze point and gaze vector representations.

- **Relative Gaze Point:** The relative gaze point is provided for the left and right eye individually and corresponds to the two dimensional position of the gaze point within the calibration plane. The coordinates are normalized to [0,1] with the point (0,0) in the upper left corner from the user's point of view.
- **Validity Code:** The validity code is an estimate of how certain the eye tracker is that the data given for an eye really originates from that eye.
- **Pupil Diameter:** The pupil diameter data is provided for the left and the right eye individually and is an estimate of the pupil size in millimeters.

3.3 SOFTWARE

3.3.1 ANTS: ANALYSIS AND TRACKING SYSTEM

As a requirement for the research studies, the experimental application will have to support two different interfaces: eye gaze input, by using the eye tracker previously mentioned, and hand movement input, by using the Analysis and Tracking System (AnTS) [40].

AnTS is a tracking tool that can process a live video stream or read from a video file to detect and track objects. The main concept behind it is that a number of filters can be applied to process the video stream, and the tracking process is performed on the resulting filtered images. The detection of objects can be done either automatically or manually by choosing the

desired target. As illustrated in Figure 8, AnTS is mainly used for simple tracking tasks in 2D, but has also been used in a rehabilitation research [41].

FIGURE 8 - Examples of the applications of the AnTS tool. Left, AnTS user interface. Right, color tracking (top) and multiple object tracking (bottom).

In the context of this research, AnTS will be used as a color tracking tool, to detect and track the hand movements of the users.

3.3.2 REHABNET CONTROL PANEL

To facilitate the integration of the interfaces with the application, RehabNet Control Panel was used (see [42] for an in-depth look at the full RehabNet platform).

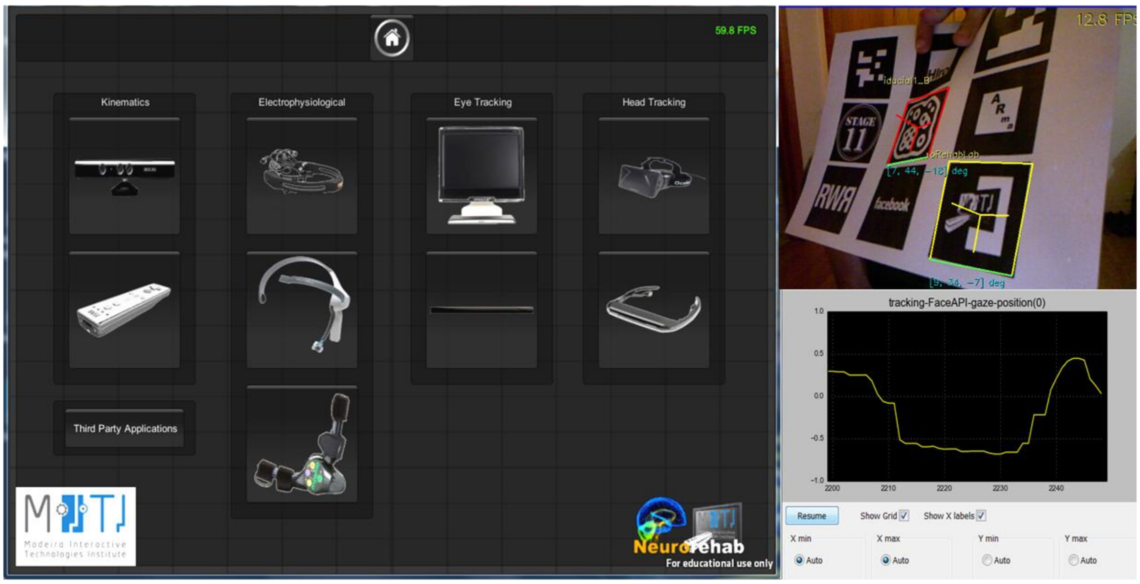

FIGURE 9 - RehabNet Control Panel. Left, RehabNet CP supported devices. Right, augmented reality tracking (top) and data visualization (bottom).

RehabNet Control Panel (CP) is a software, based on Unity, that acts as a device router, bridging a large number of tracking devices and other hardware with several games and applications developed for rehabilitation purposes [42]. RehabNet CP streams formatted data over UDP sockets and supports over 12 sensor modules, including: head-mounted displays, physiological sensors, kinematic sensors, eye tracking, face tracking, and AR tracking.

In this particular case, RehabNet CP serves as an intermediary between the chosen interfaces (eye tracker and AnTS) and the virtual task implemented in Unity (see section *3.3.3.2 Virtual Task Module* for more details). The reason for using RehabNet CP is twofold. First, it would allow the application to be incorporated with the RehabNet architecture, enabling a series of features like filtering, smoothing, translation, emulation and logging of the data collected during the task. Secondly, it would provide support for the eye tracker and AnTS (and any other device supported by the RehabNet CP if needed), making their integration into the application transparent and easier to implement.

3.3.3 Unity

Software wise, Unity[1] was the chosen platform to support the implementation of the system application. Unity is a cross-platform game creation system that can be used to create any 3D (or 2D) virtual environment. It supports JavaScript, C# and Boo programming languages, and allows for a rapid deployment of the content created on several platforms. These features, combined with its accessibility and comprehensive documentation, made it a clear choice for the implementation of the system.

Based on the defined paradigm, this section describes the application built in Unity and its integration with the eye tracking device. This integration was possible thanks to the Tobii SDK package, which can be used to access the gaze data obtained from the eye tracker. In order to maintain consistency, the implementation on the VR-ET system was done in C#, since it is supported by both the Tobii SDK and Unity.

3.3.3.1 Calibration Module

For a preliminary implementation, a calibration module was built in Unity to allow the calibration of the eye tracker directly from the application. This module was based on the calibration mode available in the Tobii Studio[2] software. The communication with the eye tracker is done directly through the Tobii SDK.

During the calibration process the eye tracker adapts its algorithms to the person sitting in front of the device, by making the user look at points located at a known set coordinates. As illustrated in Figure 10, the calibration of the eye tracker implemented uses five calibration points, and is done as follows:

1) A red, moving circle is shown on the screen to catch the user's attention.
2) When it arrives at the calibration point coordinates, the circle rests for about 0.5 seconds to give the user a chance to focus. The circle shrinks to focus the gaze.

[1] Unity includes a game engine and an integrated development environment (IDE). Version 4.3.4 was used to create the virtual task.
[2] Tobii Studio is a proprietary eye tracking analysis and visualization software that comes bundled with the Tobii Eye Tracker.

3) When shrunk, the eye tracker starts collecting data for that specific calibration point.
4) The application waits for the eye tracker to finish the calibration data collection on the current position.
5) The circle is enlarged again, and moves to the next calibration point.
6) Steps 2-5 are repeated until all calibration points are visited.

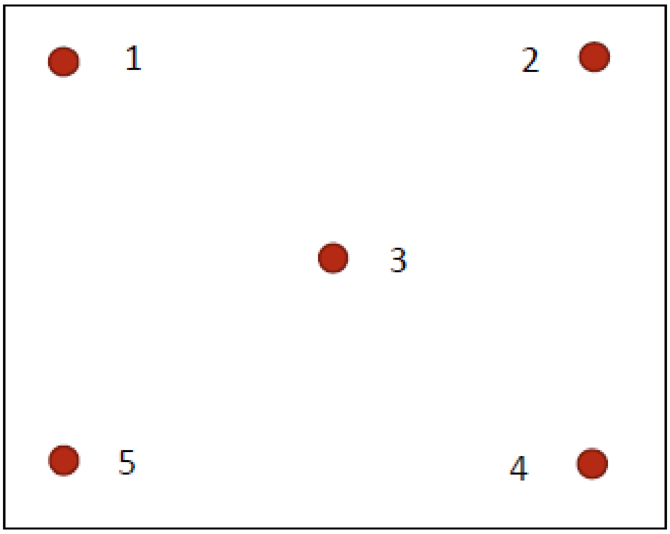

FIGURE 10 - 5-point calibration pattern used in the calibration module.

All points are given in normalized coordinates in such a way that (0.0, 0.0) corresponds to the upper left corner and (1.0, 1.0) corresponds to the lower right corner of the calibration area.

3.3.3.2 VIRTUAL TASK MODULE

The next step in the implementation process was to create a virtual task that would take into account the training paradigm described. A simple reach-grab-release task was designed and implemented in Unity. The aim was to create a clear and simple environment, rather than a visually appealing one, for a rapid and effective deployment/validation of the system. Contrary to the calibration module, this module communicates with the eye tracker through the RehabNet CP, which would allow the task to be executed not only through eye gaze but also with hand movements.

As can be seen in Figure 11, the goal of the task is to reach and grab the ball with the virtual arm, take it to the fixed target destination, and then come back to the starting position.

In terms of design elements, the virtual environment is composed of an arm, a ball, a starting point and a destination point. The environment is presented in a first-person perspective, allowing the virtual arm to be consistent with the user's point of view. The arm can be displayed on either side of the screen, simulating both left and right arm during the task.

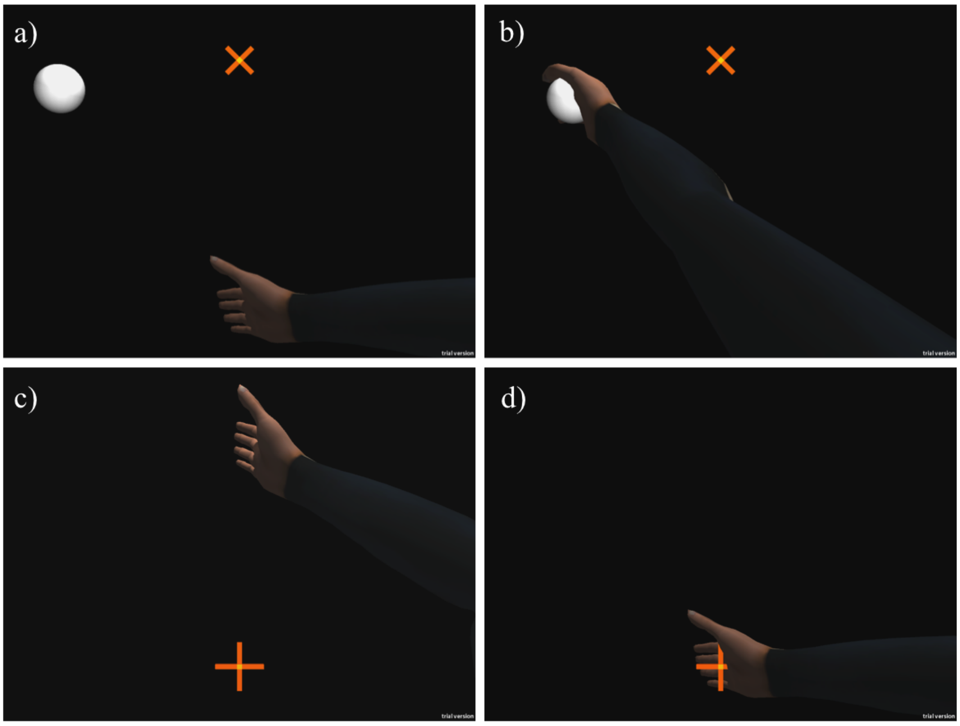

FIGURE 11 - The virtual reality task consist of 4 steps: a) reaching the virtual ball, b) grasping the ball, c) placing it at the target and releasing it, and d) moving back to the initial position.

A ball was chosen as the object to be grabbed, since it allows for a more natural grabbing motion and minimizes the cognitive load on the user. As depicted in Figure 12, there are four pre-defined points for the ball's initial position, all equidistant to the destination point and vertically symmetrical, which would randomly be chosen during the execution of the task to avoid any kind of prediction from the user.

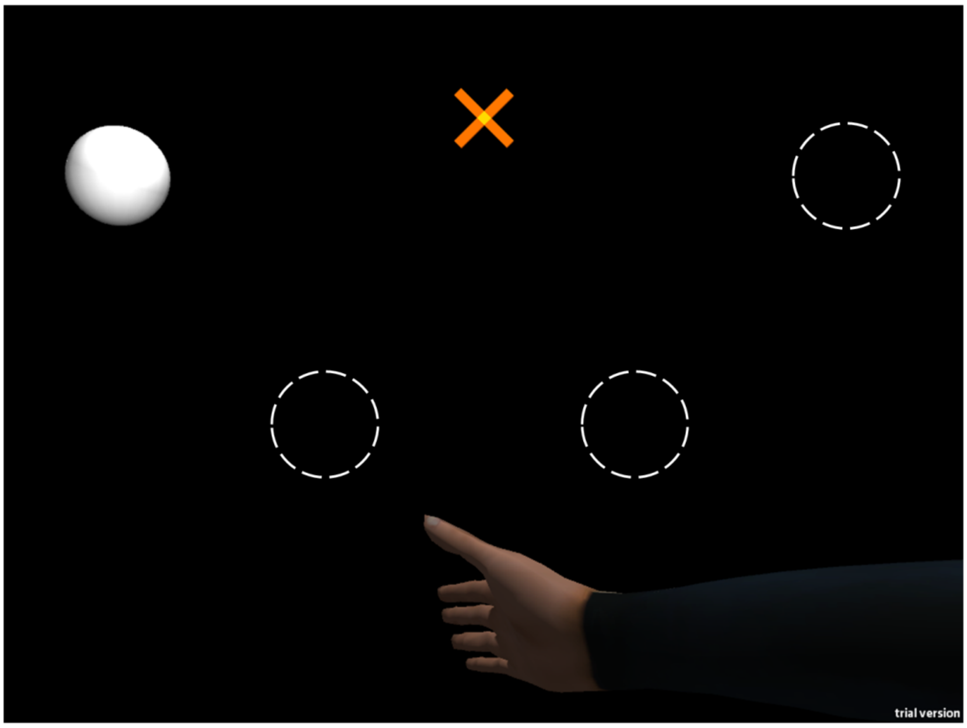

FIGURE 12 - Initial positions for the virtual ball.

For the starting and destination points, two cross-shaped objects were used, both with different orientations to allow easy differentiation between them. In the initial design the ball and both crosses were white. However, this lead to some issues in identifying the actual object to be grabbed, and as such the colors of the starting and destination points were changed in detriment to their neutrality. The surroundings of the task consist of a black background to make it as neutral as possible.

Apart from for the virtual arm, the virtual elements are not always visible on the environment. Instead, they are dynamic and depend on the actions being executed during the task (see Figure 11). The reasoning behind this decision, and most design decisions taken for this task, is the need to minimize possible attentional distractions, and concentrate the focus of attention of the user to the actual task execution. Another aspect taken into account was the fact that this task must also be executed with gaze-controlled input, and as such the interface should be as clear as possible to properly guide the user through its execution.

Starting from the initial state, the elements appear in the following way:

1) Only the ball and the destination point are visible.
2) After grabbing the ball and taking it to the destination point, these elements vanish and the starting point appears.
3) When the arm reaches the starting point and after a defined interval of time has passed, the ball and the target destination reappear while the starting point becomes invisible again.
4) This process is repeated for as many times as deemed necessary, with the ball randomly reappearing in different pre-defined positions every time.

4. Assessing the Impact of Stroke in a VR Observation and Execution Task

This chapter focuses on the first of two research studies done to explore the potential of the system developed. The contents of this chapter lead to a conference paper publication [43]. The first study was performed with post-stroke patients, and aimed at assessing the impact of stroke in action observation and action execution through eye gaze, using the VR task developed. The chapter starts by introducing the experimental hypotheses that were to be tested during the study. It follows with the methods used and the results found from the experiments done with the patients. The chapter ends with the main conclusions and relevant findings that resulted from the study.

4.1 Introduction

As seen from the state of the art, the concept of a partially shared neural network between action observation and action execution in healthy participants has been demonstrated through a number of studies [21, 22, 23, 24]. However, little research has been done in this regard using eye movement metrics in rehabilitation contexts. This study approaches action observation and action execution by combining a virtual environment and eye tracking technology.

Participants consisted of stroke survivors, and were required to perform a simple reach-grab-release task with both their paretic and non-paretic arm using the VR-ET system. The eye gaze of the participants was analyzed in a task where they observe their arm in the virtual environment while executing reaching and grasping actions, and when they control the virtual arm directly with their eye gaze[3].

Under the assumption of interference between the neuronal circuits underlying execution and observation, it is expected to detect some differences in the paretic vs. non-paretic arm conditions that may eventually be used for diagnostic and rehabilitation purposes. Essentially, the aim was to verify the following hypotheses:

a) Congruency in gaze metrics between action execution and action observation in stroke patients;
b) Differences in gaze metrics in stroke patients during action observation using their paretic arm when compared to their non-paretic arm;
c) No differences in gaze metrics in stroke patients during eye-controlled action execution when comparing the paretic to their non-paretic arm.

In order to verify these hypotheses, a series of experimental trials was conducted with stroke patients, using the VR-ET system previously presented.

[3] The initial design for the study included a third condition, where participants would use their arm to directly control the virtual arm on screen through AnTS. Hence, this is why the system was implemented with this interface in mind. However, patients presented major difficulties in executing this condition with their affected arm, and as such this condition was later discarded and not considered for the study.

4.2 METHODS

4.2.1 PARTICIPANTS

Patients with no arm mobility and/or with severe attention deficits were excluded from the study, since these conditions could have influenced their performance with the task at hand. The group that participated in the study consisted of 10 stroke survivors (5 female and 5 male), with a mean age of 66.6 years (SD = 10.6 years) and a mean of 221.2 days after stroke (SD = 157.4 days). Seven patients suffered an ischemic stroke and 3 patients suffered an intra-cerebral hemorrhage. In terms of lesion, 4 patients had a left-sided lesion and 6 patients had a right-sided lesion.

	Age (years)	Lesion side	Lesion type	Days since stroke
Participant 1	54	Left	Hemorrhagic	34
Participant 2	78	Left	Hemorrhagic	202
Participant 3	68	Right	Ischemic	474
Participant 4	78	Right	Ischemic	293
Participant 5	79	Right	Hemorrhagic	209
Participant 6	60	Right	Ischemic	140
Participant 7	52	Left	Ischemic	80
Participant 8	56	Left	Ischemic	489
Participant 9	62	Right	Ischemic	80
Participant 10	74	Right	Ischemic	211

TABLE 2 - Clinical characteristics of the post-stroke patients who participated in the study.

All the participants were naive to the system and hypotheses being tested, and supplied written informed consent (see Appendix A - Participants Consent Form) prior to participation. Patients were recruited from Hospital Dr. Nélio Mendonça and Hospital Dr. João de Almada, located in the Funchal area. The study was approved by the Ethical Committee of the Regional Health System of Madeira (SESARAM; see Appendix B - Ethics Approval).

4.2.2 SETUP

The VR-ET system was used to display the virtual environment and record the eye movements of the participants at a sampling rate of 60 Hz. A laptop computer connected to the eye tracking device ran the custom VR software during the trials.

As can been seen in Figure 13, participants sat in front of the eye tracker, with their heads at around 60 cm distance from the screen, and both hands over the table in front of them. The VR environment, shown in the eye tracker display, presented the user with a virtual arm that performed a sequence of movements.

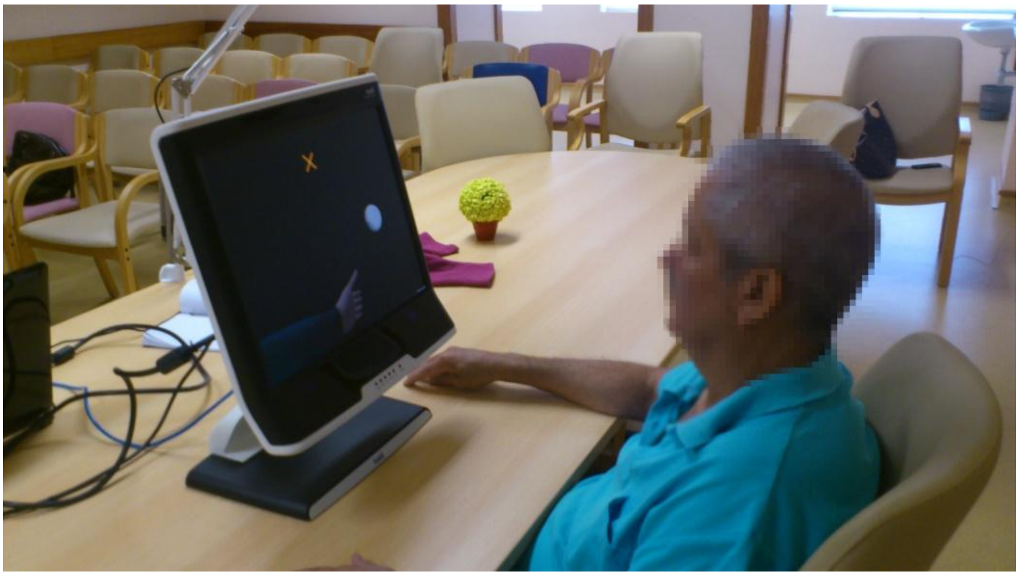

FIGURE 13 - Experimental setup being used by a stroke patient.

In order to study the proposed hypotheses, the system was used in two different configurations: action observation and eye-controlled action execution. In the particular case of the action execution, the eye movements data is fed back to the system to control the movements of the virtual arm. For both conditions, the eye gaze data and virtual arm movements were collected for later analysis.

4.2.3 PROCEDURE

Participants were presented with a simple reach-grab-release task in the virtual environment. As illustrated in Figure 14, during the trials participants were presented with two different conditions, in the following order: i) action observation – participants were required to observe a pre-recorded execution of the virtual arm grabbing the ball and taking it to the target destination; and ii) eye-controlled action execution– participants were required to actively grab the ball with the virtual arm using their eye gaze and take it to the target destination. Prior to the action observation condition, participants were instructed to observe the task performed in such a way that they could repeat it later.

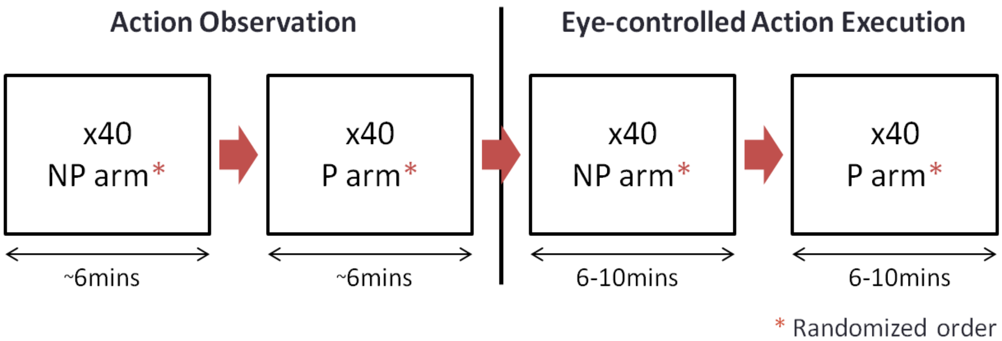

FIGURE 14 - Overview of the experimental protocol for the first study.

For each condition, each participant had to perform (or observe) 40 repetitions of the task for each arm, with each repetition lasting around 30 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. The order of the arm to use during both conditions was also randomized.

4.2.4 Statistical Analysis

All data analysis was performed with MATLAB (MathWorks Inc., Natick, USA). Eye tracking data was filtered with a Gaussian window of 1.6 seconds with *SD* = 0.16 s. Eye tracking data (X,Y) was then converted to screen coordinates. Data was removed from the segments were eye tracking data was missing and also during the resting periods.

According to the velocity profile of the data, eye tracking behavior was classified into i) fixations, ii) saccadic movements, and iii) smooth pursuit. For each behavior detected, the number of occurrences and their duration was assessed. In addition, the accumulated travelled distance was also computed.

Out of the 10 participants, 1 dataset of the action observation condition was corrupt and only 6 patients could complete the action execution task due the interference of stroke derived attentional or cognitive deficits.

The 2-sided Lilliefor test revealed that data was not normally distributed. A non-parametric test, matched pairs Wilkoxon test, was used to assess differences between paretic and non-paretic data on the same participants. To test against different conditions, where size groups differ in size (9 and 6), the non-parametric Mann-Whitney test was used to report differences.

4.3 Results

From all the participants, a total of 9 stroke patients performed successfully the action observation conditions whereas only 6 could complete the eye-controlled action execution condition.

4.3.1 Gaze Patterns

A first analysis of the data classifying eye gaze patterns into fixations, saccadic movement, and smooth pursuit movements revealed very different spatial distributions for each one (see Figure 15).

In the context of the VR task previously presented, fixations are mostly clustered around the location of targets (release place at the top-center and resting position at the bottom-center of the screen) and the virtual ball's starting positions (two on the right and two on the left halves of the screen). Saccadic movements were detected mostly between the target position and the resting position. These two positions are presented sequentially since every release at the target position is followed by a movement to the resting position to trigger the next sequence of actions. 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, which is congruent with the task at hand. Further, there is consistency when comparing eye gaze patterns between the two experimental conditions. There are no major differences between conditions and the distribution of eye gaze patterns triggered in response, finding congruent eye gaze patterns in action observation and action execution.

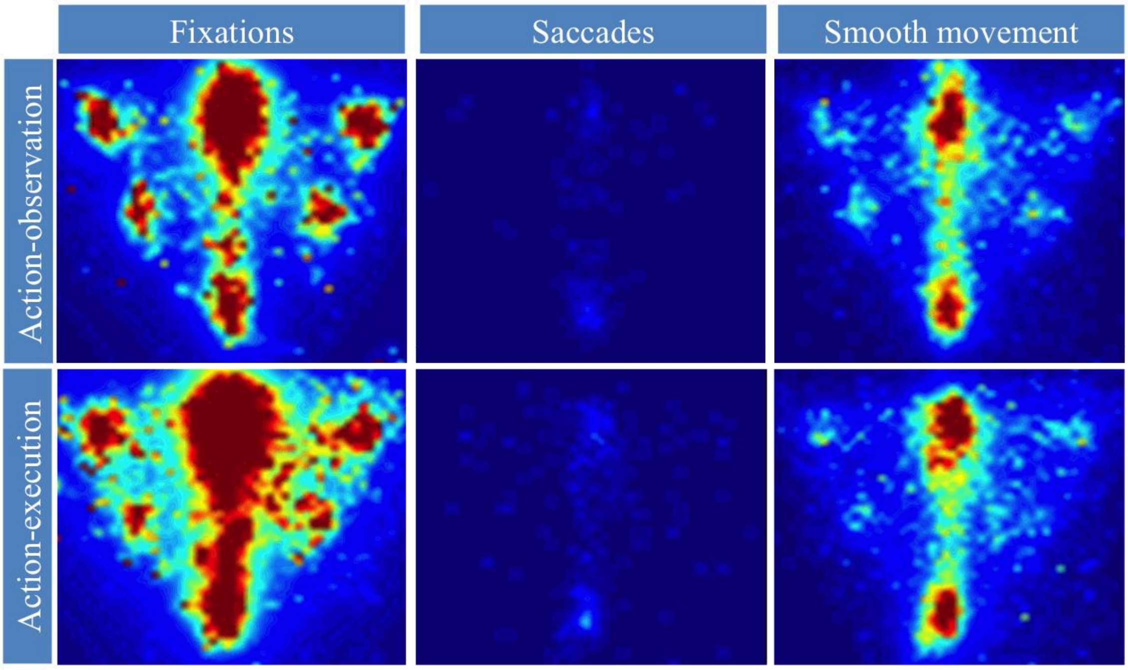

FIGURE 15 - Density maps for action observation and action execution conditions according to the detected eye movements.

4.3.2 GAZE METRICS

For the following analysis, seven different metrics extracted from the eye tracking data were used: number of fixations, saccades and smooth pursuit segments, duration of fixations, saccades and smooth pursuit segments, and the overall accumulated eye gaze distance travelled.

	Action observation		**Action execution**	
	Paretic	**Non-P.**	**Paretic**	**Non-P.**
Fixation count	**1295**	**1272**	**2955**	**3241**
Fixation duration	384 ms	376 ms	270 ms	298 ms
Saccades count	**53**	**52**	**115**	**113**
Saccades duration	271 ms	276 ms	286 ms	291 ms
Smooth pursuit count	**361**	**403**	**535**	**497**
Smooth pursuit duration	**587 ms**	**567 ms**	605 ms	589 ms
Distance	238 a.u.	283 a.u.	302 a.u.	311 a.u.

TABLE 3 - Median values of the eye gaze metric according to each condition for the paretic and non-paretic arm (a.u. stands for arbitrary units).

An analysis of the occurrence of eye gaze fixation patterns reveals clear differences between action observation (Mdn=1283) and action execution (Mdn=3241), U=252, p<0.01. Similarly, the number of saccades is significantly lower in the case of action observation (*Mdn*=52) than for action execution (*Mdn*=113), *U*=276, p<0.001. This finding is also consistent with the

occurrence of smooth pursuit patterns, with *Mdn*=364 for action observation and *Mdn*=519 for action execution, *U*=238, $p<0.05$. Thus, there is a consistent increase of the number of fixations, saccades and smooth movements in execution as compared to observation. On the contrary, no differences could be found with the available data with respect to the duration of those events, except for a tendency to longer fixations in the action observation condition. No differences were found in distance travelled either.

When performing a within subject analysis to the different eye gaze patterns in response to the presentation of the paretic vs. non-paretic virtual arm, it was found that patients do perform 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.

4.4 Conclusions

For this first study, the data shows congruency in gaze metrics between action execution and action observation in stroke patients, as far as distribution and duration of gaze events validating the first hypothesis (a). However, the observed increase in the number of events may indicate large differences between observation (open loop eye gaze) and execution (closed loop eye gaze) systems. These differences could also be explained by the longer duration of the eye-controlled task, since the participants were not familiar with eye gaze interface and took longer to execute it.

In the action observation condition, patients performed longer smooth pursuit when observing movements of the virtual arm corresponding to their paretic arm. This difference could be explained by the recruitment of motor control areas of the brain affected by stroke, which is consistent with the second proposed hypothesis (b).

However, in the eye-controlled action execution condition no differences were found between paretic and non-paretic arm presentation. Consistent with the last hypothesis (c), this could indicate that eye-controlled execution does not involve, at least to a large extent, the neural mechanisms of motor control affected by stroke, because it may not engage motor areas to predict how the virtual arm will move.

With these findings, further evidence that recruitment of motor areas occurs during observation was shown. Which suggests that observation can be used as a valid rehabilitation tool. Furthermore, gaze metrics can also be used as diagnostic to quantify impairment in post-stroke patients, and as a tool to monitor the rehabilitation of stroke.

5. ASSESSING HEALTHY BEHAVIOR IN A VR OBSERVATION AND EXECUTION TASK

This chapter presents the second research study performed as a follow-up to the first one. This study was conducted in order to evaluate the normal gaze behavior in action observation and action execution with healthy participants. The chapter starts by introducing the hypotheses being tested during the study. It continues with the methods used and then presents the results obtained from the trials with healthy participants. The chapter concludes with the discussion and relevant findings that were taken from the experiments.

5.1 INTRODUCTION

From the first study with post-stroke patients, some doubts arose about the fact that arm dominance may have had some influence on the results found during action observation. However, this could not be verified with the data from the study, since the motor deficits presented by the patients would interfere with the comparison of arm dominance. There was also an interest in trying to simulate the motor limitations as consequence of stroke in healthy participants, to analyze their gaze metrics in such condition and compare them to their normal behavior. As a result, a second study with healthy participants was conducted, not only to verify arm dominance influence but also to compare healthy behavior with the VR task created in normal conditions and under simulated motor impairment. Furthermore, the study aims to verify if the simulated impairment through movement constrain also affects eye gaze.

Participants were required to perform the same reach-grab-release task used in the previous study, through the VR-ET system. The eye gaze of the participants was analyzed during the task where they observe their dominant and non-dominant arms in the virtual environment when executing reaching and grasping actions, and when they control the virtual arm directly with their eye gaze.

For this study, the objective was to verify the following hypotheses:

a) Differences in gaze metrics during action observation using their dominant arm when compared to their non-dominant arm;
b) No differences in gaze metrics during eye-controlled action execution when comparing the dominant to their non-dominant arm;
c) Differences in gaze metrics during normal condition versus constrain-induced condition.

To verify these hypotheses, a series of experimental trials was conducted with healthy participants, using the VR-ET system.

5.2 METHODS

5.2.1 PARTICIPANTS

A sample of 20 participants (3 female and 17 male) was recruited for the study, with a mean age of 30.4 years (SD = 6.5 years). All but one participant were right handed. Participants were

naive to the system and hypotheses being tested, and supplied written informed consent prior to participation.

5.2.2 SETUP

The same setup used in the previous study was used again. The VR-ET system displayed the virtual environment and recorded the eye movements of the participants at a sampling rate of 60 Hz. The eye gaze data and virtual arm movements were collected for later analysis.

5.2.3 PROCEDURE

Participants were presented with a simple reach-grab-release task in the virtual environment, and the configurations of the previous study were used: action observation and eye-controlled action execution. Prior to the action observation condition, participants were instructed to observe the task performed in such a way that they could repeat it later. In addition, participants had to perform these in two different conditions: normal condition and constrained condition (see Figure 16).

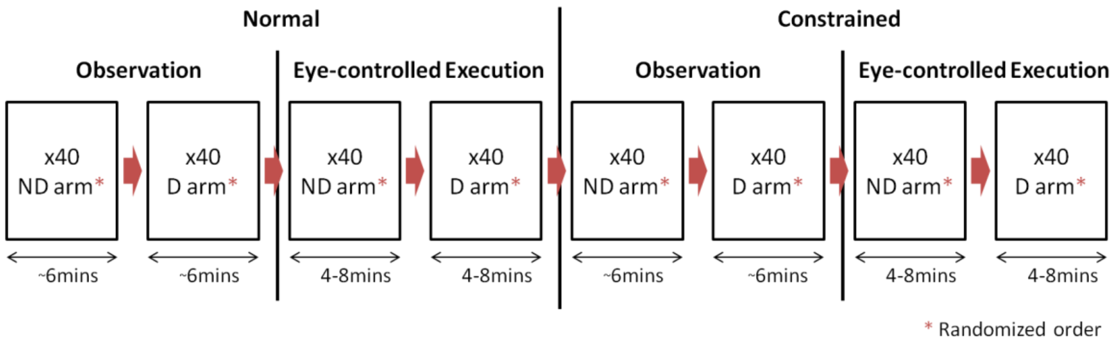

FIGURE 16 - Overview of the experimental protocol for the second study.

For the normal condition, participants simply sat in front of the eye tracker with their heads at around 60 cm distance from the screen, and both hands over the table in front of them. For the constrained condition, a similar setup was used except participants had one of their hands and elbows constrained in accordance to the virtual arm being displayed (e.g. if the left arm was being displayed during the task their left hand and elbow were constrained). The order of the conditions was randomized between participants during the trials.

5.2.4 STATISTICAL ANALYSIS

All data analysis was performed with MATLAB. Eye tracking data was filtered with a Gaussian window of 1.6 seconds with SD = 0.16 s. Eye tracking data (X,Y) was then converted to screen coordinates. Data was removed from the segments were eye tracking data was missing and also during the resting periods.

According to the velocity profile of the data, eye tracking behavior was classified into i) fixations, ii) saccadic movements, and iii) smooth pursuit. For each behavior detected, the number of occurrences and their duration was assessed.

A non-parametric test, matched pairs Wilkoxon test, was used to assess differences between dominant and non-dominant data on the participants, and also to assess differences between constrained and non-constrained conditions.

5.3 RESULTS

5.3.1 GAZE PATTERNS

A first analysis of the data classifying eye gaze patterns into fixations, saccadic movement, and smooth pursuit movements revealed different spatial distributions for each one in the normal condition (see Figure 17) and constrained condition (see Figure 18).

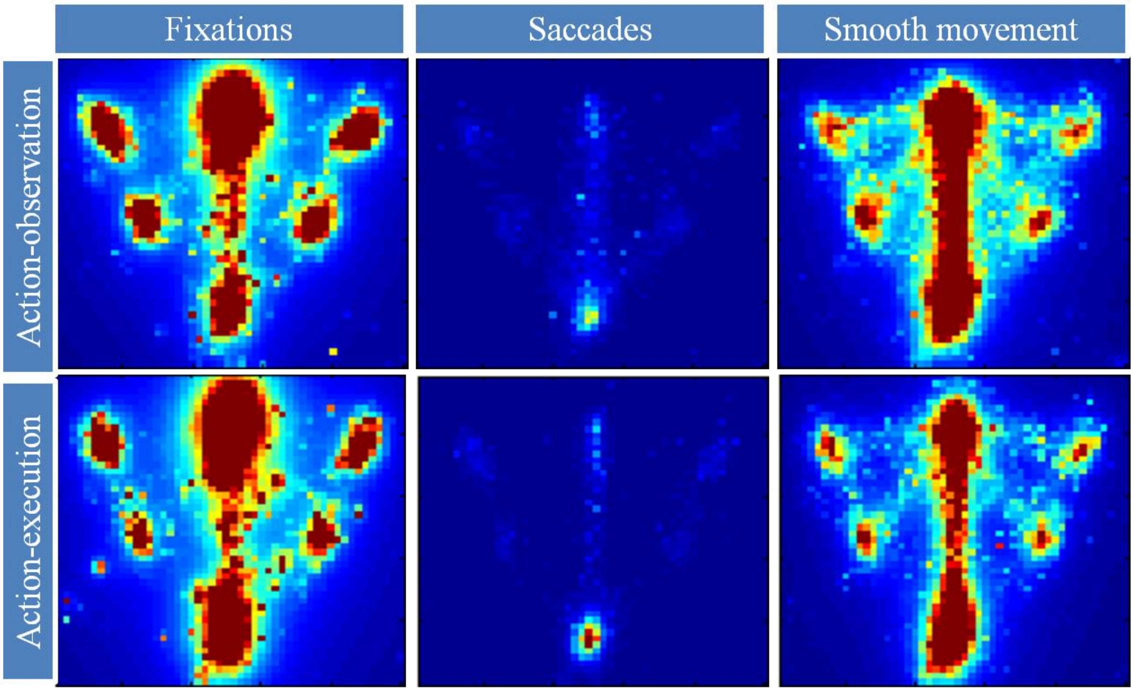

FIGURE 17 - Density maps for action observation and action execution according to the detected eye movements in the normal condition.

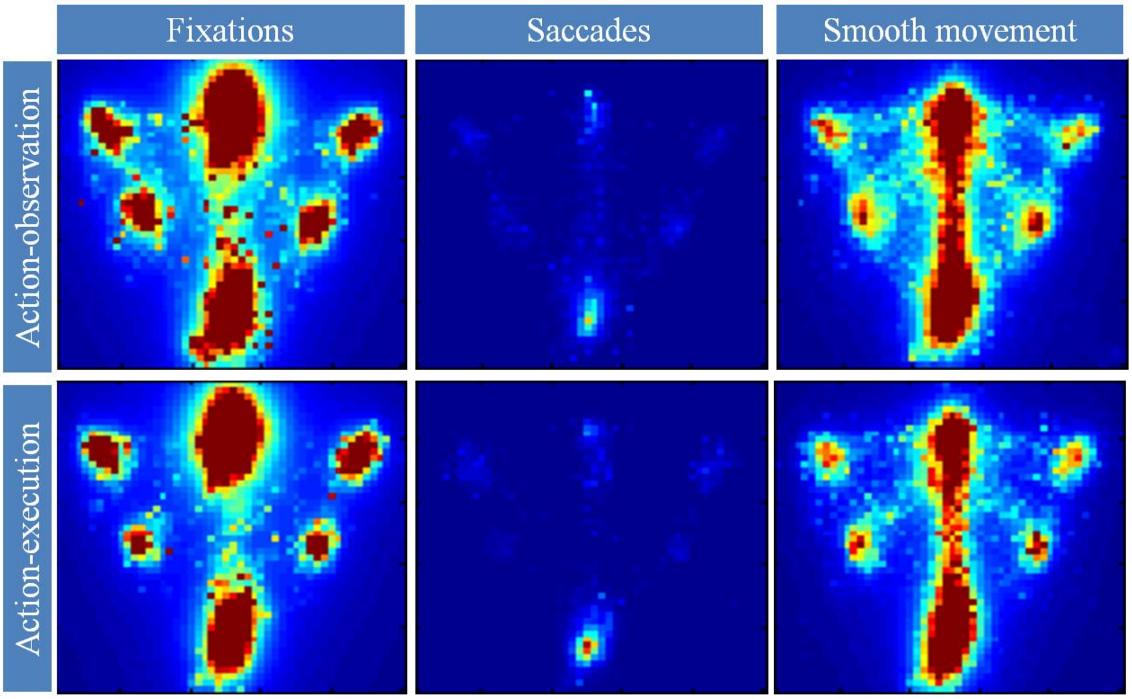

FIGURE 18 - Density maps for action observation and action execution according to the detected eye movements in the constrained condition.

The results for the gaze patterns' spatial distribution are similar to those found in the previous study in both the non-constrained and constrained conditions. Fixations are mostly clustered around the location of the release place and the resting position, and the ball's starting positions. Saccadic movements were detected mostly between the target position and the resting position. Smooth pursuit events are detected mostly in the areas between virtual objects and their respective targets. In this case, there is still consistency when comparing eye gaze patterns between action observation and action execution. When comparing the normal condition and constrained condition, there are no major differences in the distribution of eye gaze patterns triggered in response.

5.3.2 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.

	Action observation		**Action execution**	
	Dominant	**Non-D.**	**Dominant**	**Non-D.**
Fixation count	**1309***	1243	1367	1241
Fixation duration	**234 ms**	210 ms	**249 ms**	**305 ms***
Saccades count	58	60	58	56
Saccades duration	**265 ms**	**291 ms**	265 ms	**268 ms**
Smooth pursuit count	**314**	**379**	226	**260**
Smooth pursuit duration	**621 ms**	577 ms	**663 ms**	685 ms

Table 4 - Median values of the eye gaze metric according to each configuration for the dominant and non-dominant arm, in the normal condition.

	Action observation		**Action execution**	
	Dominant	**Non-D.**	**Dominant**	**Non-D.**
Fixation count	**1061***	1261	1142	1263
Fixation duration	243 ms	174 ms	305 ms	**235 ms***
Saccades count	58	59	54	51
Saccades duration	**272 ms**	**275 ms**	**255 ms**	**259 ms**
Smooth pursuit count	307	320	211	228
Smooth pursuit duration	**560 ms**	**604 ms**	**654 ms**	**630 ms**

Table 5 - Median values of the eye gaze metric according to each configuration for the dominant and non-dominant arm, in the constrained condition.

When comparing action observation with action execution, the analysis reveals the following significant differences in the gaze metrics. In the normal condition and considering the dominant arm only, the fixation duration is longer in action execution (*Mdn*=249 ms) than in action observation (*Mdn*=234 ms), p<0.05. The same occurs for the smooth pursuit duration, with *Mdn*=663 ms for action execution and *Mdn*=621 ms for action observation, p<0.05. Considering the non-dominant arm, the saccades duration is shorter in action execution (*Mdn*=268 ms) when compared to action observation (*Mdn*=291 ms), p<001. Differences were also found in the smooth pursuit count, with less events occurring in action execution (*Mdn*=260) than action observation (*Mdn*=379), p<0.001.

In the constrained condition and considering the dominant arm, the saccades duration are shorter in action execution (*Mdn*=255 ms) compared to action execution (*Mdn*=272 ms), p<0.05, while the duration of smooth pursuit is longer in action execution (*Mdn*=654 ms) than in action observation (*Mdn*=560 ms), p<0.05. The same results were observe for the non-dominant arm, with shorter saccades duration in action execution (*Mdn*=259 ms) compared to action observation (*Mdn*=275 ms), p<0.01, and longer smooth pursuit duration in action execution (*Mdn*=630 ms) compared to action observation (*Mdn*=604), p<0.01.

When performing a within subject analysis to the different eye gaze patterns in response to the presentation of the dominant versus non-dominant arm, results showed that participants perform shorter saccades when observing the dominant arm (*Mdn*=265 ms) than when observing the non-dominant arm (*Mdn*=291 ms), p<0.01, and less smooth pursuit events when observing the dominant arm (*Mdn*=314) compared to the non-dominant arm (*Mdn*=379), p<0.05. No other differences could be found between dominant and non-dominant arm.

Finally, comparing the normal condition and constrained condition, it was found that shorter fixation duration occur in the constrained condition (*Mdn*=235 ms) when compared to normal condition (*Mdn*=305 ms), p<0.01, and also that fixations are less likely to occur in the constrained condition (*Mdn*=1061) than compared in the normal condition (*Mdn*=1309), p<0.05. No other significant differences were found between these conditions.

5.4 Conclusions

For the second study, data shows consistency in gaze metrics between action execution and action observation in both the constrained and non-constrained conditions, as far as distribution and occurrence of gaze events. However, there is a consistent increase in smooth pursuit duration and a decrease in saccades duration in action execution, across constrained and non-constrained conditions. Similar to the previous study, these differences may indicate a distinction between the observation (open loop eye gaze) and execution (closed loop eye gaze) systems.

Despite the differences found when comparing the eye gaze metrics between dominant versus non-dominant arm, validating the first hypothesis (a), no differences were found for smooth pursuit duration in observation. This fact supports the results previously found, by showing that differences found between the paretic and non-paretic arm in the observation condition in the first study (differences in smooth pursuit duration) were not due to arm dominance, but to the recruitment of motor control areas of the brain affected by stroke.

In the eye-controlled action execution condition no differences were found between dominant and non-dominant arm presentation in either the constrained and non-constrained conditions. Consistent with the second hypothesis (b) and reinforcing the results found in the first study, this could indicate that eye-controlled execution does not engage motor areas to predict how the virtual arm will move.

The differences shown between the constrained and non-constrained condition are consistent with the last hypothesis (c). This demonstrates that simulating the motor limitations of post-stroke patients in healthy participants may affect their eye gaze during observation and eye-controlled execution of a goal-oriented task.

Although several results were found that supported the hypotheses formulated in both the first and second study, the exploratory approach taken for these studies is limited. In fact, no justification could be found to explain why differences occurred in those particular gaze metrics and conditions, since there is no clear model that can explain how these metrics relate to the brain processes underlying the actions performed. Therefore, a model-driven hypothesis verification is needed to better understand the relation between neuronal mechanisms and eye gaze metrics in goal-oriented tasks.

6. Towards a Model-driven Paradigm

This chapter briefly presents the groundings for a new model-driven evaluation paradigm, resulting from the findings of the two research studies conducted. The chapter starts by introducing this paradigm in the research context, and then proposes two possible approaches that aim at creating a model for such paradigm, that could be used in future research.

6.1 Introduction

As concluded in the two previous chapters, the exploratory approach used for the research studies was valuable but limited. The studies verified the existence of significant differences in gaze metrics in the tested conditions, showing evidence that the affected motor areas in stroke patients could affect eye movements during goal-oriented tasks. Given that a detailed model about the relationship between eye gaze and motor function does not yet exist, no conclusions could be made about why the differences were found in those particular metrics and conditions.

In order to better understand these findings, a better model that explains how these metrics relate to goal-oriented actions needs to be defined. Such model should follow a set of strict and unambiguous specifications that would allow for a clear relation between gaze metrics and actions performed.

The following sections propose two model-driven approaches, based on eye tracking and virtual reality, for which a model-driven rehabilitation paradigm can be created.

6.2 Trajectory-based Approach

It is known that eye gaze performs continuous predictions of the behavior of a followed target. As such, the main focus of this first approach is to evaluate how different object trajectories can influence the gaze prediction of an observer. The general idea is to quantify the eye movements of an observer when a stimulus that changes its behavior over time is presented. The changes can evolve from a linear trajectory (easier to predict) to the superposition of multiple non-linear trajectories (more difficult to predict).

As a first implementation of this approach, a proof of concept was designed and created in Unity. A virtual environment presents to the user a moving object that follows a trajectory that changes over time. The trajectory is customizable through a set of parameters (see Figure 19), and can range from a simple linear movement to a more complex multilevel trajectory.

The eye gaze data recorded during the observation of these movements is used to extract gaze metrics, similar to those used in the research studies, which in turn provide information on the reliability of gaze prediction as a function of target behavior. This information can then be incorporated into a diagnostics task that assesses gaze prediction according to the complexity of an object trajectory.

FIGURE 19 - Proof of concept of the trajectory-based approach with the customizable parameters for the trajectory of the object.

6.3 OBJECT-BASED APPROACH

This second approach focuses on evaluating how the nature of different objects can influence gaze prediction and response time when observing/executing a goal-oriented task. This hypothesis is based on the understanding that mirror neurons respond selectively to the type of grasp or object that is being interacted with. Therefore, if a particular population of mirror neurons specialized in fine/power grasp or in a particular type of object are impaired, this should be reflected on the observation of these tasks.

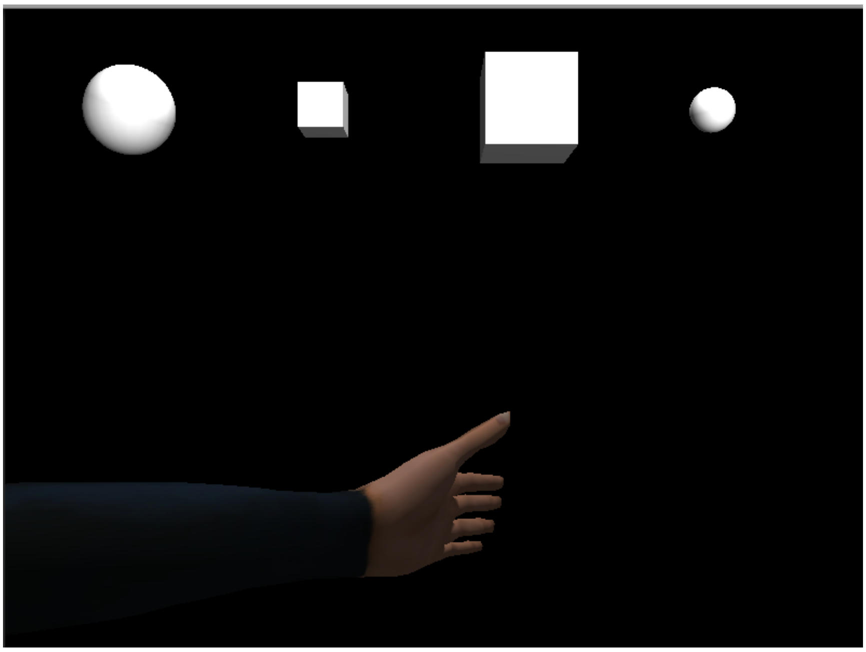

FIGURE 20 - Concept for an implementation of the object-based approach.

The main concept is to design a reach-and-grab task (see Figure 20), in line with the one created for the research studies, in which the user is presented with several objects of varying sizes, shapes or colors. The goal of the task would be to reach and grab a specific object among the ones presented. The gaze metrics extracted from the gaze data collected could provide valuable information on the gaze behavior, and could be incorporated into a diagnostics task that assesses gaze prediction and response time according to the objects used.

6.4 Conclusions

Both proposed approaches have a solid theoretical background and can be the basis for future work in this area, since they are based on the results of the research done during this thesis.

These approaches aim at creating non-trivial models to explain how gaze behavior relates to goal-oriented actions, and therefore extend the existing range of applications of eye tracking and virtual reality in rehabilitation. Based on such model, a new model-driven paradigm could be implemented in real stroke recovery contexts, bringing potential benefits to the current rehabilitation process.

7. Discussion and Conclusion

This thesis focused in the research of novel methods of assessment and rehabilitation of post-stroke patients, by exploring the potential use of eye tracking technology in virtual reality environments.

The use of eye tracking technology has been growing over the last decades in rehabilitation research, and has shown promising results when incorporated with other technologies, like virtual reality. The concept of mirror neurons has been shown to play an important part in the neural mechanisms during action execution and action observation. Furthermore, evidence that action observation has a positive effect on the recovery of motor deficits has been proven, leading to a significantly higher impact than traditional neurorehabilitative techniques alone. By incorporating eye tracking and virtual reality into this concept, one could improve the current rehabilitation process, and use these technologies to create novel methodologies to assess and rehabilitate motor deficits during action execution and action observation.

Based on this approach, the VR-ET system was created to explore the potential of using eye gaze movements during observation and execution of goal-oriented tasks in a virtual environment for assessment and rehabilitation purposes. The system combined a non-intrusive eye tracking device with a custom virtual environment where the task occurred. The system would record all gaze data of the user during the task for later analysis.

Two research studies were conducted with VR-ET system to get a better understanding of the gaze patterns that resulted from observing and executing a goal-oriented task, in stroke patients and healthy participants. One of the studies lead to a conference paper [43] and an invitation for a publication with the Methods of Information in Medicine Journal.

The first study was done with post-stroke patients across two hospitals. Participants were required to observe and perform (with their eye gaze) a simple reach-grab-release task with both their paretic and non-paretic arm representations. Results showed congruency in gaze metrics between action execution and action observation, for distribution and duration of gaze events. Significant differences were found in the gaze metrics between the paretic and non-paretic when patients observed the task being done. This may be explained by the recruitment of motor control areas of the brain affected by stroke, and suggests that eye tracking can be used to assess motor deficits derived from stroke in action observation.

The second study was conducted with healthy participants also using the VR-ET system, and aimed at understanding the effects of arm dominance in gaze metrics during a goal-oriented task, as well as comparing the gaze behavior of healthy patients in constrained and non-constrained conditions. Despite some differences found in gaze metrics between dominant versus non-dominant arm, none of them interfered with the results found in the previous study. This reinforced the fact that the recruitment of motor control areas of the brain affected by stroke may indeed explain the differences found previously. Results also showed that simulating the motor limitations of post-stroke patients in healthy participants could affect their eye gaze during goal-oriented tasks.

Even though several results were found that supported the hypothesis formulated in both studies, the exploratory approach taken for these studies was limited. For instance, no explanation could be found as to why differences occurred in those particular gaze metrics and experimental conditions. Therefore, a model-driven paradigm is needed to better understand the relation between the neuronal mechanisms underlying goal-oriented actions and eye gaze metrics. Two approaches, based on eye tracking and virtual reality, were proposed to model this relation and serve as a stepping-stone for future research in this area.

Overall, one could say that the goal set for this thesis was accomplished. The research went beyond the current state of the art and proposed a novel system with potential to be used as an assessment and rehabilitative tool for post-stroke patients. The system can also be extended to further increase the understanding of eye gaze's role in stroke rehabilitation. With the increasing availability of low-cost eye tracking devices, a system like the one created can become a cost effective solution for at home rehabilitation of people suffering from motor disabilities.

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APPENDIX

APPENDIX A - PARTICIPANTS CONSENT FORM

DOCUMENTO DE CONSENTIMENTO INFORMADO

Entendo que toda a informação derivada do estudo "Sistema interativo para diagnóstico e reabilitação de défices cognitivo-motores: ensaio clínico longitudinal controlado em pacientes com Acidente Vascular Cerebral" é propriedade da equipa de investigação responsável. Dou o meu consentimento para que dados anónimos a meu respeito (resultados, imagens e vídeos) possam ser guardados e processados para fins de avaliação científica. Li (foi-me lida) a informação mencionada acima. Entendo o significado desta informação, e as minhas perguntas foram satisfatoriamente respondidas. Tive tempo suficiente para decidir sobre a participação neste estudo. Venho por este meio consentir a minha participação e consentir na recolha, uso e revelação de informação. Irei receber uma cópia deste documento de consentimento informado assinada e datada.

______________________ Assinatura do participante	__________ Data
______________________ Nome do Representante legal - se aplicável	__________ Data
______________________ Nome do Investigador	__________ Data

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APPENDIX B - ETHICS APPROVAL

2013/11/21

UNIVERSIDADE da MADEIRA

CA
Autorizado
17/4/01/03

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Serviço de Saúde da RAM, E.P.E
ENTRADA
E.A363647 2013/11/21
Classificação: 18.69

21/11/13

Exmo. Senhor Miguel Ferreira, Presidente do Conselho de Administração do SESARAM,

Como investigador responsável do projeto *"Sistema interativo para diagnóstico e reabilitação de défices cognitivo-motores: ensaio clínico longitudinal controlado em pacientes com Acidente Vascular Cerebral"*, em parceria com o Dr. Rafael Freitas, a Dra. Teresa Maria Fernandes Gois Bento e a Dra. Manuela Barros do hospital Nélio Mendonça, venho por este meio pedir o parecer e autorização da Comissão de Ética para a Saúde para a realização deste estudo no âmbito do projeto RehabNet: NEUROSCIENCE BASED INTERACTIVE SYSTEMS FOR MOTOR REHABILITATION, aprovado pela comissão europeia com a referência 303891 FP7-PEOPLE-2011-CIG.

Com os melhores cumprimentos,

Sergi Bermúdez i Badia
Prof. Aux. Universidade da Madeira

REGIÃO AUTÓNOMA DA MADEIRA
SERVIÇO DE SAÚDE DA REGIÃO AUTÓNOMA DA MADEIRA, E.P.E.

Comissão de Ética para a Saúde do SESARAM,EPE
(CES/SESARAM,EPE)

PARECER Nº47/2013

Sobre o Pedido/Estudo: "***Sistema interativo para diagnóstico e reabilitação de défices cognitivo-motores: ensaio clínico longitudinal controlado em pacientes com Acidente Vascular Cerebral***"

A - RELATÓRIO

A.1. A Comissão de Ética para a Saúde (CES) do Serviço de Saúde da Região Autónoma da Madeira, EPE (SESARAM,EPE) iniciou a análise do Documento Nº 02 da reunião de 25 de Novembro de 2013, enviado pelo Conselho de Administração para parecer, relativo a pedido de autorização de **Sergi Bermúdez i Badia**, Professor Auxiliar da Universidade da Madeira, e investigador responsável do projeto "***Sistema interativo para diagnóstico e reabilitação de défices cognitivo-motores: ensaio clínico longitudinal controlado em pacientes com Acidente Vascular Cerebral***", em parceria com o **Dr. Rafael Freitas**, a **Dra. Teresa Góis Bento** e a **Dra. Manuela Barros**, do Hospital Dr. Nélio Mendonça, para a realização deste estudo no âmbito do projeto RehabNet: NEUROSCIENCE BASED INTERACTIVE SYSTEMS FOR MOTOR REHABILITATION, aprovado pela comissão europeia com a referência 303891 FP7-PEOPLE-2011-CIG.

A.2. Fazem parte do documento em avaliação: ofício ao Presidente do Conselho de Administração do SESARAM,EPE e Projeto de Investigação que inclui Documento de Informação ao Sujeito da Investigação e Documento de Consentimento Informado.

A.3. Trata-se de um estudo que propõe o desenvolvimento de um sistema interativo computadorizado baseado em Realidade Virtual que englobe um leque diversificado de tarefas para a reabilitação de défices cognitivo-motores após lesão cerebral, tais como: défices motores, de memória, linguagem, atenção e funções executivas. A avaliação clínica cognitiva consistirá na aplicação de um conjunto de escalas aferidas (ou em aferição) para a

população portuguesa e terá por objectivo a avaliação das diferentes capacidades cognitivas. Esta avaliação será efetuada pela psicóloga do projeto, Ana Lúcia dos Santos Faria, aluna de doutoramento no M-ITI. A avaliação motora consistirá de um conjunto de escalas standard para avaliar diferentes capacidades a nível motor e funcional. Esta avaliação será efetuada pelo médico interno Jean-Claude Fernandes ou outros avaliadores designados pelo SESARAM. Para analisar a reorganização das áreas cerebrais motoras dependendo do tratamento realizado, os investigadores pretendem realizar ressonância magnética funcional aos pacientes envolvidos no estudo antes e depois do tratamento (*baseline* e semana 12). Os pacientes com AVC serão recrutados em unidade de saúde do SESARAM. Serão avaliados pacientes agudos/sub-agudos, visto ser nesta fase que ocorre a maior parte da reorganização cerebral pós-lesão, sendo por isso o período em que o impacto da reabilitação é mais pronunciado; também serão avaliados pacientes numa fase crónica pós-AVC. Os pacientes serão devidamente informados dos objetivos, relevância e pormenores do estudo e tratamento, e serão convidados a participar no estudo de forma voluntária. Todos os pacientes que aceitem participar no ensaio clínico devem dar o seu consentimento informado verbal e escrito segundo o modelo em anexo. Os pacientes podem em qualquer momento interromper de forma voluntária a participação no estudo. Pretende-se recrutar para cada intervenção (motora e cognitiva) 40 pacientes com AVC (20 para sistema interativo + 20 para controlo). Para investigar o impacto da tecnologia proposta na recuperação de pacientes vítimas de AVC, serão realizados testes de usabilidade e vários ensaios clínicos controlados. São critérios de inclusão: primeiro episódio de AVC (em qualquer uma das suas etapas); AVC isquémico com afectação cognitiva e com ressonância magnética/tomografia computadorizada identificando a localização e características da lesão; capacidade cognitiva suficiente para a compreensão e execução das tarefas: Mini Teste do Estado Mental ≥15[Folstein, Folstein et al. 1975;Guerreiro,Silva et al. 1994]; Escolaridade ≥4.ª classe ou saber ler e escrever; Idade: 30-75 anos; Cooperação e motivação para participar voluntariamente neste estudo.

Os pacientes que preencham os critérios de inclusão serão aleatoriamente alocados a um dos grupos de tratamento [Intervenção ou Controlo], assegurando-se a homogeneidade dos grupos. Os resultados deste estudo serão apresentados de forma explícita através de tabelas e gráficos. A análise de dados será realizada usando MATLAB 2008ª [MathWorksInc., Natick, MA, USA] e SPSS 16.0 [SPSS Inc. Chicago, IL, USA]. No que respeita a proteção de dados, nomes, datas de nascimento e outros dados sensíveis e passíveis de identificação serão encriptados para proteger a privacidade do paciente e dos dados recolhidos; a informação recolhida será utilizada apenas para o propósito do projeto e não será retida para outros fins; nenhuma informação pessoal será tornada pública ou cedida a terceiros; serão aplicados controlos técnicos estritos para garantir que a informação não seja disponibilizada inadvertidamente a organizações de marketing direto ou outras terceiras entidades.

B- IDENTIFICAÇÃO DAS QUESTÕES COM EVENTUAIS IMPLICAÇÕES ÉTICAS

B.1. Estão dadas garantias de confidencialidade e anonimato dos participantes.

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 - CONCLUSÃO

A CES deliberou dar **Parecer Favorável** ao presente estudo, nos precisos termos em que o mesmo foi apresentado, por não se colocarem quaisquer questões de ordem ética.

Aprovado em reunião do dia 25 de Novembro de 2013, por unanimidade.

O Presidente da CES/SESARAM,EPE

(Ricardo Santos)

REGIÃO AUTÓNOMA DA MADEIRA – COMISSÃO DE ÉTICA – SERVIÇO REGIONAL DE SAÚDE, E.P.E.