



Development and applicability assessment of a rehabilitation plan for Hemispatial Neglect patients using Augmented Reality

Ricardo Manuel Esperança de Brito

Thesis to obtain the Master of Science Degree in

Biomedical Engineering

Supervisors: Prof. Ana Luísa Nobre Fred Prof. Dr. Hugo Alexandre Teixeira Duarte Ferreira

Examination Committee

Chairperson: Prof. João Miguel Raposo Sanches Supervisor: Prof. Ana Luísa Nobre Fred Members of the Committee: Prof. Paulo Luís Serras Lobato Correia

December 2020

Preface

The work presented in this thesis was performed at the company NEVARO (Lisbon, Portugal), during the period March-December 2020, under the supervision of Prof. Hugo Ferreira from Instituto de Biofísica e Engenharia Biomédica. The thesis was co-supervised at Instituto Superior Técnico by Prof. Ana Fred.

Declaration

I declare that this document is an original work of my own authorship and that it fulfills all the requirements of the Code of Conduct and Good Practices of the Universidade de Lisboa.

Acknowledgements

Os meus primeiros agradecimentos dirigem-se à minha família que, durante toda a minha vida, e principalmente nos últimos 5 anos, me deu um apoio incondicional, não só durante a realização da tese de mestrado, mas durante todo o curso, e garantiu que sempre tive todas as condições para poder ser a melhor pessoa e aluno que consigo ser. Aos meus amigos, expresso também a minha gratidão por estarem sempre ao meu lado e por tornarem o meu percurso numa experiência que irei para sempre recordar.

Ao terminar o curso de Engenharia Biomédica, é-me possível olhar para trás e perceber que foram estas pessoas que me moldaram na pessoa que sou hoje. Um enorme obrigado a todas.

Em termos curriculares, quero deixar uma palavra de agradecimento à Prof.^a Ana Fred por ter aceite o cargo de orientadora interna e ao Prof. Hugo Ferreira pela sua disponibilidade para o cargo de orientador externo. As suas contribuições foram fundamentais e, apesar da atual situação pandémica, fizeram todos os possíveis para me auxiliar, transmitindo-me conhecimento e apoiando-me sempre que necessário.

Às Engenheiras Francisca Canais e Rita Maçorano da Nevaro e ao Doutor Pedro Alves do Hospital de Santa Maria quero também demonstrar o meu profundo agradecimento por possibilitarem a realização desta dissertação em parceria com a start-up Nevaro, incutindo um cariz prático e uma proximidade com o mundo empresarial que enriqueceu bastante a minha experiência. Além disto, asseguraram-se sempre que reunia todas as condições para poder realizar a minha dissertação da melhor maneira possível.

Por último, deixo também um obrigado a todas as pessoas que despenderam do seu tempo para participar neste estudo e agradeço em especial ao Francisco Cachado, por me ter ajudado incansavelmente durante a realização desta dissertação.

O mais sincero agradecimento a todos.

Abstract

The impact of Hemispatial Neglect is clear. Since it is a consequence of stroke, namely right hemispheric stroke, its prevalence is significant, affecting the lives of numerous people (approximately 240 000 people in a year in the acute phase of the disease in the USA alone). Moreover, it is a highly impairing disease which deeply compromises self-sufficiency, autonomy and restricts the day-to-day capabilities of the patient.

The current study conducts a comprehensive analysis of the disease and the underlying brain regions where lesions often lead to the appearance of symptoms; identifies the currently used rehabilitation and therapy strategies to tackle the disease, proposes a novel strategy for the rehabilitation of Hemispatial Neglect patients using Augmented Reality and auditory stimuli and tests its applicability on healthy individuals.

The results obtained, namely the qualitative results, identify some improvements to be implemented to the strategy proposed but, nonetheless, substantiate its applicability since the results and the feedback were positive. The participants performed all tasks with ease and no adverse reaction was observed. The quantitative results, although not the main focus of this research, also highlight useful details which should be considered prior to clinical application of the strategy. Once the aforementioned improvements are incorporated, the solution will be ready for the next research phase – application on Hemispatial Neglect patients.

Keywords: Stroke; Hemispatial Neglect; Augmented Reality; Virtual Cueing; Visual and Auditory Cueing

Resumo

O impacto da Negligência Hemispacial é claro. Uma vez que é uma consequência de AVC, nomeadamente AVC no hemisfério cerebral direito, a sua prevalência é significativa, afetando a vida de inúmeras pessoas (prevalência anual estimada de 240 mil pessoas na fase aguda da doença apenas no Estados Unidos da América). Além disso, é uma doença muito limitante que compromete bastante a autossuficiência, autonomia e restringe até as capacidades mais simples do paciente.

O presente estudo realiza uma análise abrangente da doença e das regiões cerebrais onde lesões frequentemente levam ao aparecimento de sintomas, identifica as estratégias de reabilitação e terapia atualmente utilizadas para combater a doença, propõe uma solução inovadora de reabilitação de Negligência Hemispacial usando Realidade Aumentada e estímulos auditivos e testa a sua aplicabilidade em indivíduos saudáveis.

Os resultados obtidos, nomeadamente os resultados qualitativos, identificam algumas melhorias a ser implementadas na estratégia proposta, mas, não obstante, comprovam a sua aplicabilidade uma vez que os resultados e o *feedback* foram positivos, os participantes realizaram todas as tarefas sem dificuldade e não foram observadas quaisquer reações adversas. Os resultados quantitativos, apesar de não serem o foco principal do estudo, também realçam pormenores importantes que devem ser considerados antes da aplicação clínica da estratégia. Após a incorporação das melhorias referenciadas anteriormente, a solução estará pronta para a próxima fase de investigação – aplicação em pacientes com Negligência Hemispacial.

Palavras-Chave: Negligência Hemispacial; Realidade Aumentada; Estímulos Virtuais; Estímulos Visuais e Auditivos; Acidente Vascular Cerebral

Contents

Preface	ii
Acknowledgements	iv
Abstract	vi
Resumo	viii
Contents	1
List of Figures	3
List of Tables	4
Glossary	5
1. Introduction	6
1.1 Motivation	6
1.2 Hemispatial Neglect	6
1.2.1 Etiology	7
1.2.2 Prevalence	7
1.2.3 Symptomatology	8
1.2.4 Diagnosis	8
1.2.5 Physiology	10
1.2.6 Treatment	10
1.3 State-of-the-Art	11
1.3.1 Cueing applied to Hemispatial Neglect Rehabilitation	11
1.3.2 Virtual Reality and Augmented Reality	14
1.3.3 VR/AR cueing applied to Hemispatial Neglect Rehabilitation	15
1.4 Objectives and Proposed Approach	
1.4.1 Novel Contributions	19
1.5 Thesis Overview	19
2. Methodology and Experimental Setup	20
2.1 Phase 1 – Preliminary Tasks	21
2.1.1 Line Bisection	21
2.1.2 Cancellation Task	21
2.1.3 Clock Test	22
2.1.4 Article Reading	22
2.2 Phase 2 – Virtual and Auditory Cueing	23

2.2.1 Visual Cues	23
2.2.2 Auditory Cues	25
2.2.3 Outline of Phase 2	25
2.3 Phase 3 – Task Repetition	27
2.4 Game Experience Questionnaire	27
2.5 Data Collection and Analysis	28
3. Results	30
3.1 Line Bisection	30
3.2 Task Cancellation	31
3.3 Clock Test	32
3.4 Article Reading	33
3.5 Phase 2	33
3.6 Game Experience Questionnaire	34
4. Discussion	36
5. Conclusion	42
5.1 Future Work	43
6. References	45
7. Appendices	51
7.1 Appendix A. Exercise Sheets, Phase 1	51
7.2 Appendix B. Exercise Sheets, Phase 3	54
7.3 Appendix C. GEQ and Results Sheet	58
7.4 Appendix D. Informed Consent and Informative Sheet	61

List of Figures

FIGURE 1: DRAWING OF A CLOCK BY A PATIENT WITH HEMISPATIAL NEGLECT	8
FIGURE 2: EXAMPLE OF TEMPLATES TO PERFORM THE CANCELLATION TASK (LEFT) AND TELLING AND SETTING THE TIME (RIGHT)	
DESCRIBED IN THE TEXT.	9
FIGURE 3. MEAN ERROR IN THE LINE BISECTION TEST. BOTH THE VISIBLE AND INVISIBLE CUES WERE SHORT VERTICAL LINES. HOWE	VER,
FOR THE INVISIBLE CUES, THE RESEARCHER PRETENDED TO DRAW THE LINE USING A LEADLESS PENCIL IN FRONT OF THE	
participant. [24]	12
FIGURE 4: SEARCH EFFICIENCY AS A FUNCTION OF SOUND CONDITION. ONE STAR INDICATES THE LOWEST SEARCH EFFICIENCY AND	тwo
STARS THE HIGHEST	12
FIGURE 5: PARTICIPANT THREE'S BELL TEST SCORE	16
FIGURE 6: PARTICIPANT THREE'S BIT BEHAVIORAL SUBTEST SCORES.	17
FIGURE 7: PARTICIPANT THREE'S BIT CONVENTIONAL SUBTEST SCORES.	17
FIGURE 8: LOCATIONS WHERE THE SOLUTION WAS APPLIED, AND THE RESULTS WERE OBTAINED (MAP CREATED WITH MICROSOFT	
Power BI [60])	
FIGURE 9: DEMONSTRATION OF THE FIRST AR GAME - THE RED SPHERES FLASH UNI OR BILATERALLY, TO BE IDENTIFIED BY THE	
PARTICIPANT, AND MOVE TOWARDS THE PERIPHERY OVER TIME. THE BOTTOM CUE SERVES AS SUPPORT TO HELP UNDERSTAI	ND
THE PURPOSE OF THE GAME.	24
FIGURE 10: DEMONSTRATION OF THE SECOND AR GAME - THE DIFFERENT SHAPES FLASH SEQUENTIALLY IN RANDOM AREAS OF TH	ŧΕ
FoV, to be identified by the participant. The bottom cue serves as support to help understand the purpose o	F THE
GAME	24
FIGURE 11: GOGGLES USED FOR THE AR TASKS	25
FIGURE 12: HEAT MAP REPRESENTING THE ABSOLUTE ERROR DISTRIBUTION BEFORE AND AFTER PHASE 2	31
FIGURE 13: CLOCK DRAWN BY ONE OF THE PARTICIPANTS (J.B.) COMPARED TO THE ACTUAL CLOCK PRESENTED.	33
FIGURE 14: SCORES FOR EACH COMPONENT IN THE GAME EXPERIENCE QUESTIONNAIRE [42] (THE UPPER PART PRESENTS THE SCO	ORES
FOR THE POST-GAME MODULE; THE LOWER PART CONTAINS THE SCORES FOR THE CORE MODULE).	
FIGURE 15: DURATION OF EACH TASK, IN MINUTES. THE DURATION OF THE LINE BISECTION, TASK CANCELLATION, CLOCK TEST AI	ND
ARTICLE READING IN THE GRAPH SHOW THE SUM OF THEIR DURATION IN PHASE 1 AND 3.	35
FIGURE 16: ONE OF THE PARTICIPANTS PERFORMING THE AR TASKS.	40
FIGURE 17: LINE BISECTION EXERCISE SHEET FOR PHASE 1	51
FIGURE 18: CANCELATION TASK EXERCISE SHEET FOR PHASE 1.	52
FIGURE 19: CLOCK TEST EXERCISE SHEET FOR PHASE 1	52
FIGURE 20: ARTICLE READING EXERCISE SHEET FOR PHASE 1	53
FIGURE 21: LINE BISECTION EXERCISE SHEET FOR PHASE 3.	54
FIGURE 22: CANCELATION TASK EXERCISE SHEET FOR PHASE 3.	55
FIGURE 23: CLOCK TEST EXERCISE SHEET FOR PHASE 3	56
FIGURE 24: ARTICLE READING EXERCISE SHEET FOR PHASE 3.	57
FIGURE 25: GAME EXPERIENCE QUESTIONNAIRE	58
FIGURE 26: FIRST AND SECOND PAGES OF THE RESULTS SHEETS	59
FIGURE 27: PART OF THE THIRD AND FOURTH PAGES OF THE RESULTS SHEET.	
FIGURE 28: FIRST PAGE OF THE INFORMED CONSENT.	
FIGURE 29: SECOND PAGE OF THE INFORMED CONSENT	62
FIGURE 30: THIRD PAGE OF THE INFORMED CONSENT.	
Figure 31: First page of the Informative Sheet.	
FIGURE 32: SECOND PAGE OF THE INFORMATIVE SHEET	-
FIGURE 33: THIRD PAGE OF THE INFORMATIVE SHEET.	

List of Tables

TABLE 1: RESULTS OBTAINED FROM THE LINE BISECTION TEST FOR EACH PARTICIPANT (IN MILLIMETERS) BEFORE AND AFTER PHASE	2.
	30
TABLE 2: RESULTS OBTAINED FROM THE TASK CANCELLATION FOR EACH PARTICIPANT BEFORE AND AFTER PHASE 2.	31
TABLE 3: RESULTS OBTAINED FROM THE CORE MODULE OF THE GAME EXPERIENCE QUESTIONNAIRE	34
TABLE 4: RESULTS OBTAINED FROM THE POST-GAME MODULE OF THE GAME EXPERIENCE QUESTIONNAIRE	34

Glossary

AR	Augmented Reality
BIT	Behavioral Inattention Test
СТ	Computed Tomography
EEG	Electroencephalogram
FoV	Field-of-View
HMD	Head Mounted Display
HN	Hemispatial Neglect
Hz	Hertz
LB	Line Bisection
PET	Positron Emission Tomography
SPECT	Single Photon Emission Computed Tomography
тс	Task Cancellation or Cancellation Task
VR	Virtual Reality

1. Introduction

1.1 Motivation

Hemispatial Neglect (HN) is a highly harming disease which affects the lives of a large number of people worldwide (approximately annual prevalence of 240 000 people in the acute phase of the disease in the USA alone). The consequences of this condition often translate into the daily lives of the patients, both during their hospitalization and afterwards, restricting their capabilities and autonomy, further increasing the impairment. So, an effective tool for hastening the rehabilitation process is very important. The treatment of HN is still not consensual. Thus, it is imperative to gain in-depth understanding of this pathology to better adapt to it and develop effective treatment plans. Furthermore, with the emergence of technologies such as Augmented Reality (AR), the opportunities for treating visuospatial diseases expanded remarkably. Incorporating these state-of-the-art tools in the rehabilitation strategies for patients with HN is still a revolutionary concept and, thus, remains in early works but the possibilities are extremely promising and should be explored.

1.2 Hemispatial Neglect

The disease of HN, also known as Hemineglect, Unilateral Neglect or Unilateral Spatial Neglect, is a neuropsychological condition that follows an injury sustained in one or both hemispheres of the brain and is characterized by a disorder of attention where patients typically fail to orientate, report or respond to stimuli located on one side of space and may also compromise other senses, like touch, hearing, smell or pain. The term "Hemispatial" derives from the fact that one half of the field-of view (FoV) is disregarded. The symptoms tend to alleviate naturally but the time required differs greatly between patients and can take up to several months. Unlike most cognitive disorders, Hemineglect has been found in different species of mammals [1]. Even though some cases of ipsilesional hemineglect have been reported, the vast majority of the patients suffer from contralesional unilateral neglect - the side of the field of view affected is the opposite of the brain hemisphere that sustained the lesion and so, patients have a tendency to prioritize objects in the same side as their brain damage [2]. Most cases of hemineglect occur after a lesion on the right hemisphere of the brain (up to 80% of right brain hemisphere strokes lead to some degree of unilateral neglect - more specifically, strokes affecting the territories irrigated by the large middle cerebral artery, right inferior parietal lobe or the temporo-parietal junction) and so, there is a tendency for the left side of space to be disregarded. A possible justification may be the fact that the right hemisphere of the brain is specialized in shape recognition, spatial perception, and memory while the left hemisphere is mostly responsible for analytic thought and language. [3] [4]

Lesions in the frontal lobe tend to cause more transient types of neglect. Several other brain regions have been shown to be connected to HN when damaged, but with less robust results (small patient sample and further research is required), such as the angular gyrus of the parietal lobe, right

basal ganglia, parahippocampal region (a region which connects the parietal cortex and the hippocampus – responsible for spatial orientation) or medial temporal lobe. A study conducted by Leibovitch et al. tested a sample of 120 patients with a single right-hemisphere-damaged lesion using a Computed Tomography (CT) exam and 88 of those patients also with a SPECT exam. This experiment concluded not only that structural and functional imaging techniques with neurobehavioral analysis may be a helpful tool in understanding HN but also that the main brain regions associated with this pathology are the parietal and anterior cingulate cortex and white fiber bundles. Several different types of lesions and brain areas have been associated with HN and, thus, it varies between patients and many different mechanisms are considered to contribute to this condition – disorders in directing attention, difficulty in disengaging attention and shift it leftward, impaired representation of space or directional motor impairment. Additionally, coexisting non-spatially lateralized deficits like impairments in sustained attention, selective attention, or bias to locate features in space may also contribute to HN. This inference raises new possibilities for hemispatial neglect rehabilitation since it expands to neuroscience fields which have not been considered and opens a new door for target treatments for specific deficits [3] [5].

1.2.1 Etiology

The etiology of the hemispatial neglect is vast and usually involves right hemispheric lesions. The causes include neurodegenerative diseases, traumatic brain injury or neoplasia, but the main cause of the most prominent and long-lasting neglect is right-hemispheric stroke [2][6]. A stroke happens when the supply of blood to a part of the brain is reduced or interrupted, preventing the distribution of oxygen and nutrients causing the brain cells to die within minutes (necrosis). The stroke can be ischemic (narrowing or blockage of blood vessels) or hemorrhagic (rupture or leakage in blood vessels). Thus, the etiology of hemineglect also expands to the risk factors of stroke, which may be related to lifestyle (sedentarism, obesity, drinking or drug abuse) or health conditions (high blood pressure, cholesterol, diabetes, or cardiovascular diseases). Lack of bloody supply causes cell necrosis, which has dire consequences for the patient [7].

1.2.2 Prevalence

The stroke is a highly incident, awfully impairing pathology – it is the second leading cause of death and a major cause of disability worldwide [8]. In 2016, over 80 million people in the world had experienced a stroke and around 13.7 million new strokes happen each year. Moreover, one in every four people over the age of 25 will have a stroke in their lifetime and older generations are more prone to suffer this impairment [9]. Additionally, numerous studies have shown that, although left-hemisphere strokes are more frequent, the difference is small [10] [11]. Neglect occurs in around 75% to 80% of patients in the chronic phase after right-hemispheric stroke, leading to an estimated total annual prevalence of 240 000 patients in the acute phase in the United States alone [1]. Thus, and since the Hemispatial Neglect is a consequence of stroke (both ischemic and hemorrhagic), the prevalence of both pathologies is undoubtedly associated.

1.2.3 Symptomatology

The severity of the neglect varies greatly between patients and it is unrelated to its duration. The symptoms can range from the unawareness of sensory stimuli in the contralesional side of the field of view (sensory neglect), ignoring the contralesional side of memories or internally generated images (representational neglect), lack of awareness of the contralesional side of the body (personal neglect) but the most common and significative symptoms are motor neglect (failure of limb activation as a response to a stimulus) and spatial neglect (failure to acknowledge the side of the space opposite to the brain lesion) [12]. This can translate in failing to acknowledge people or objects in the neglected side of the field of view, reading from only one side of a paper, drawing only one half of a picture (as represented in Figure 1), or eating from only one half of a plate. Additionally, many patients are unaware that they suffer from this condition (anosognia), which further increases the impairment [3].

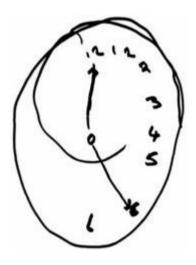


Figure 1: Drawing of a clock by a patient with hemispatial neglect.

1.2.4 Diagnosis

To assess the extent of the pathology, numerous tests have been developed in order to enable a standardized quantification. Different batteries of tests have been developed since single tasks alone are not able to diagnose HN in all patients. One of the most useful tests is the Cancellation Test. There are many versions available of this test but generally, the patients are asked to find a specific object among a varying number of distracters in the left, center, and right sides of the sheet. Tests where the subject searches for 2 target symbols are believed to be more sensitive when informing about HN. Patients with HN usually fail to detect stimuli on the side of the page opposite the brain lesion (contralesional disorder). The severity of the neglect is quantified according to the number of non-identified objects in the side of lesion when compared to the healthy side and whether distracters were selected. One of the most used Cancellation Test is the Bells Test, where the object to be searched by the patient is a Bell, with distracters ranging from trees to birds [13]. Another extremely used test is the Bisection Test – the subject is asked to mark the middle point of a line. In this test, the patients usually

mark the center of the line with a bias towards the lesioned side of the brain because the contralesional side of the field of view tends to be disregarded. The score is based on the deviation of the bisection to the midpoint. Additionally, in order to increase the significance of the results provided by these exams, they should be gualitatively evaluated - by observing the patient during the completion of the previous tests and focusing on how they perform the tasks (where the patient starts the task (left, right, top or bottom), the scanning process (methodical or unmethodical) or the task completion time), to obtain a more comprehensive report regarding the severity and extent of the pathology. Additionally, the Behavioral Inattention Test (BIT) is a test battery which allows a significative measurement of the impact of neglect on peripersonal tasks (around the subject). It is composed of 15 items: 6 Conventional tasks (line bisection, letter cancellation, star cancellation, figure copying, line bisection and free drawing) and 9 Behavioral tasks (picture scanning, telephone dialing, menu reading, article reading, telling and setting the time, coin sorting, address and sentence copying, map navigation, and card sorting) - Figure 2 represents two exercises from the BIT (the letter cancellation and telling and setting the time). The score is based on the number of omissions, distortions, or asymmetries in every subtest. However, since the majority of the previous tests require visual scanning and manual identification, they do not distinguish between visual (lack of awareness) and motor neglect (inability of moving toward the contralesional side). To distinguish between these types of neglect, scales such as the Semi-Structured Scale for Functional Evaluation of Hemi-Inattention were developed (where the subject is asked to perform tasks such as hair combing, serving tea, dealing cards or describing the environment to inform about the spatial/visual neglect). Other tests can provide quick and useful measures, such as copying and drawing tasks or asking the subject to recall certain memories (where the contralesional side of the memory is often omitted) [2] [3] [12].

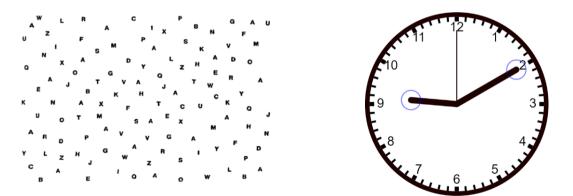


Figure 2: Example of templates to perform the Cancellation Task (left) and Telling and Setting the Time (right) described in the text.

However, before assessing the extent of the hemispatial neglect, it is important to determine whether there are present other visual pathologies, such as hemianopia or extinction, to better understand the condition of the patient and determine the best possible approach to promote their recovery. Although these illnesses may be present in neglect patients, they can be individually diagnosed and dissociated. Hemianopia, which is an illness that impacts only the visual capabilities of the patient through symptoms like distorted sight, double vision, visual hallucinations or reduced capacity to recognize stimulus, is also usually a consequence of stroke although its causes range from brain tumors to epilepsy or traumatic brain injury. Depending on its etiology, this pathology can be treated without the need of medical interference. Clinically, it differs from hemineglect since in hemianopsia the patient sustains a loss of field of view in the contralesional space (rather than a lack of attention) after a lesion occurs in the area of the posterior cerebral artery (rather than, usually, the middle cerebral artery). Additionally, patients can more accurately recall memories, can more easily fixate their gaze to the center of the field of view and cues have residual rehabilitation effects when compared to Hemineglect patients [3] [14] [15]. Extinction, with similar causes as hemianopsia, is characterized by the patient's inability to acknowledge stimulus in the contralesional side of the field of view when presented simultaneously with ipsilesional stimulus but being able to correctly identify them when presented individually [16]. All these pathologies may influence the patient's symptoms, possibly biasing conclusions and plummeting the pace of the rehabilitation. Thus, an early identification of any pre-existing visuo-spatial disorders allows the development of a more effective treatment plan.

1.2.5 Physiology

The physiological signals, namely the signals obtained with electroencephalography (EEG), of patients with hemispatial neglect differ from healthy subjects. The EEG is a non-invasive exam which measures the electrical activity of the brain through electrodes placed along the scalp and may aid in the diagnosis of cerebral lesions. It captures 5 main types of brain waves: delta (0.4 to 4 Hz, present when sleeping), theta (4 to 8 Hz, related to deeply relaxed states), alpha (8 to 12 Hz, present in relaxed and passive states), beta (12 to 35 Hz, related to anxiety, active states and external attention and alertness) and gamma waves (higher than 35 Hz, related to concentration). [17]

A study published in 2012 by Brinson [18] analyzed the EEG profile of 9 patients who previously suffered a stroke and exhibited hemispatial neglect. The results reported two important findings. Firstly, Brinson reported that HN patients have decreased beta activity, which is consistent with the attention and alertness deficits inherent to this pathology, with no significant changes in other types of brain waves. Lastly, his research also laid foundations for the modulation of the EEG exam to improve the symptoms of HN through increased beta activity.

A study published earlier by Watson et al. [19] also reported EEG slowing across the entire brain hemisphere where the stroke occurred.

1.2.6 Treatment

The rehabilitation and treatment of patients with HN has been a relevant concern due to the high prevalence of strokes worldwide (second leading cause of death). Different approaches have been investigated, both pharmacological and behavioral. Pharmaceutical treatments focus on dopaminergic therapies using medication such as levodopa, amphetamines, noradrenergic drugs, or cholinergic compounds. Yet, this approach has produced non consistent results, reducing its applicability [3]. Behavioral treatment ranges from sustained attention (encouraging patients to direct their attention to the lesioned space) [20] to trunk rotation [21], unilateral eye patching (spectacles occluding the non-lesioned space) [22], overall limb activation [23] or prism adaptation (the patient with left hemineglect initially wears a prism which displaces the vision rightward, inducing an error in this direction. Then,

when the patient adapts to this new condition, the prism is removed, leaving the patient with a leftwards error, reducing the neglect) [2]. However, of the previously mentioned therapies, the most effective one is still not consensual since the results lack robustness, and the most promising results are obtained with cueing.

The effects of using cues for improving the condition of patients with hemispatial neglect has been thoroughly investigated and the positive outcomes are recognized and optimistic. Numerous experiments in this area have shown notable improvements regarding increased attention to the neglected side of the FoV, efficacy in recruiting spatial attention and transfer of these improvements to the daily lives of the patients [22] [24] [25] [26].

The main types of cues that have been investigated are visual and auditory. Nevertheless, other types of cues have been tested such as tactile, proprioceptive or olfactory [22] [27] [28] but further research is required.

1.3 State-of-the-Art

1.3.1 Cueing applied to Hemispatial Neglect Rehabilitation

As aforementioned, the vast majority of the cases of HN happen after a lesion is sustained in the right hemisphere of the brain - this is the hemisphere of the brain responsible for spatial attention [29]. Since this pathology is most frequently contralateral, the left side of the field of view is often harmed. Therefore, the cues that provide the best results are the ones which either stimulate the right hemisphere of the brain or the left side of the field of view – so far, auditory, and visual cues produce the most robust outcomes. To confirm this hypothesis regarding visual cues, Olk et al. [24] conducted an experiment on 12 patients with hemispatial neglect, where these patients underwent the line bisection test. In fact, the results showed that a cue presented at one end of the line biases bisection performance to that side of the line – a cue on the right side of the line biases the estimation to the right and the same happens on the left. More specifically, the typical rightward bisection errors exhibited by neglect patients when bisecting horizontal lines tend to decrease with unilateral left cues and are usually enhanced with unilateral right cues (Figure 3) – cues on the left side of the line increase the bias and attention to the harmed side of the field of view, reducing the neglect-induced error while unilateral right cues have the contrary effect. Several studies corroborated this information, reassuring the efficiency and positive impact of visual cueing [26] [30] [31].

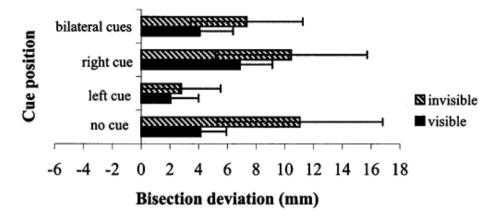


Figure 3. Mean error in the line bisection test. Both the visible and invisible cues were short vertical lines. However, for the invisible cues, the researcher pretended to draw the line using a leadless pencil in front of the participant. [24]

Additionally, Olk et al. also reported that the improvements using visible and invisible cues were similar and proportional (the invisible cues were presented by drawing a short vertical line with a leadless pencil). This supported the fact that cueing reduces hemispatial neglect based on a bias on the attention of the participant towards the cue rather than an alteration of their perception of space.

To confirm the hypothesis regarding auditory cues, Hommel et al. [27] analyzed the impact of auditory stimuli on patients with hemispatial neglect. A comparison between verbal and nonverbal cues was performed and the results showed that only the nonverbal stimuli produced significant improvements in symptom amelioration. In fact, the nonverbal sounds are processed in the right side of the brain, which suggests that these types of cues stimulate the lesioned part of the brain, reducing neglect. Further studies confirmed these conclusions, which compared the impact of classical music, white noise, and no auditory cues on patients with HN. The largest developments were reported under classical music and white noise conditions (non-verbal stimuli) [32]. A different study conducted by Van Vleet and Robertson took the analysis of auditory stimuli even further. This cross-modal experiment investigated the impact of auditory cues on the amelioration of HN symptoms and the results were consistently positive. For instance, the patient was asked to identify a target object and ignore distracters while listening to auditory beeps of 1000 Hz, 60 dB and 2000 msec of duration.

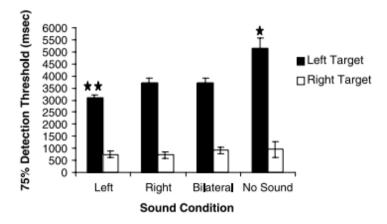


Figure 4: Search efficiency as a function of sound condition. One star indicates the lowest search efficiency and two stars the highest.

These cues were provided congruently (left) or incongruently (right) with the target or bilaterally and the results showed that auditory cues increased the search efficiency (Fig. 4). [25]

The application of nonverbal auditory cues to patients with hemispatial neglect is, therefore, an area with several possible beneficial outcomes. It is then possible to conclude that the application of verbal and/or auditory cues has a high rehabilitation potential when applied to Hemineglect patients.

The promising window of opportunity provided by cueing for the quick and effective rehabilitation of patients with hemispatial neglect is clear. As previously mentioned, the most notable improvements are obtained with visual and auditory cues. The transfer of the improvements to the daily life of the patients has also been reported. In a study conducted by Samuel et al., two patients with severe hemispatial neglect following a unilateral right hemisphere stroke were examined. These patients underwent an exam where their left limb was activated by asking the patients to prevent a noise (auditory cue) by pressing a switch in their affected side of view. It is important to note that the condition of both patients was constant for 3 months prior to this intervention. Then, after the experiments, the subjects showed notable improvements in the Bisection test, Behavioral assessment (using the *Catherine Bergego* Scale – a scale used to evaluate the existence and extent of unilateral neglect during observations of a patient [33]) and limb activation. Additionally, these changes were still noticeable during the follow-up, up to 1 month afterwards. A possible hypothesis to justify these promising reports may be the fact that left arm anchoring cues like the ones used in this experiment increase the left body space awareness and capability of recruiting motor activation in the harmed side of the body, inducing long-lasting changes in spatial attention [22].

Different theories have been presented to justify the positive impacts of cueing in Hemineglect patients. For instance, and even though the exact brain regions responsible for their activation are still not clear, the two most important neurophysiological processing components have been dissociated in this pathology: the spatial component (responsible for recognizing objects in the three-dimensional space) and the motor component (responsible for accurately recruiting motor function). Cueing may reduce the dysfunction regarding these components together by promoting the patients to direct their attention to the lesioned side of the body, increasing spatial and motor activation [1]. Other experiments offer different explanations: cueing increases the metabolic activity in the right brain hemisphere; cueing may activate cerebral pathways complementary to the harmed ones [1] [27] and cueing stimulates arousal which may increase spatial attention [32].

A number of other studies report the beneficial impact of cueing in patients with hemispatial neglect, namely in terms of error reduction in different tests such as the Bisection test or increased capacity in recruiting spatial and nonspatial attention. Moreover, some evidence also reports the transferability of these improvements into the lives of the patients outside the health facilities and a sooner return to pre-morbid conditions [22][26].

Nonetheless, using cues for the healthy rehabilitation of HN patients has a few underlying limitations. Even though some improvements can be noted in the follow-up of patients who underwent cueing, several deteriorations are present and so, there is a noticeable difficulty in consolidating the

developments. Also, the cueing approach is a subjective process due to considerable variability between patients and, thus, it is essential to tailor the approach to each patient. Therefore, a way to provide cues while decreasing the variability of learning between patients and increasing the rate of consolidation of the improvements overtime should be explored.

1.3.2 Virtual Reality and Augmented Reality

The virtual reality concept appeared in the 20th century and it is becoming affordable and more widespread in the beginning of the 21st century. It can be defined as a three-dimensional, life-sized, computer generated environment which can be explored and interacted with by the user. By using a range of hardware including Head Mounted Displays (HMD) or omni-directional treadmills, the Virtual Reality (VR) technology can provide the user with a sense of presence in a different environment. To achieve this level of immersiveness, the VR experience corresponds to our physiology and matches our senses, namely by matching the movement of the eyes and head to a perspective transformation in real-time with reduced latency (time between the action of the user and it's reflection in the virtual environment should be lower than 50 ms for a seamless experience) or shifting sound orientation according to the user's motion. The potential applicability of this technology is immense in fields such as entertainment (video games or movies), medicine (for practicing surgery, patient diagnosis or remote interventions), aviation (for pilots to practice), architecture (virtual modeling) or psychology/health – previous studies have reported that, by using this technology as a form of exposure therapy, patients with different phobias, psychological conditions or visual-spatial problems have shown improvements [34].

It is still an evolving concept – the ensuing challenges lie in developing more efficient tracking systems, further and better ways for the user to interact with the setting and decreasing the complexity of building virtual environments. Nonetheless, VR technology builds a promising ground for further developments, since it provides an easily adjustable and customizable application in terms of environment, objects and stimuli, originating a user-oriented experience with abundant benefits [35].

On the other hand, augmented reality (AR), instead of creating a whole new virtual environment to replace the real one, it adds layers and objects of digital information to the actual world – this means that, when using this technology, the user is aware of being in his/her real environment, while seeing it superimposed with virtual images, sounds, videos or other sensory cues, changing the perception of reality. Instead of changing the environment, AR enhances reality. Augmented Reality operates in real-time and the state of immersiveness is achieved through high quality 3D virtual objects with top-notch graphics and smooth transitions presented in a large variety of hardware, such as mobile phones, handheld devices, smart glasses/lenses, or HMD. This technology may provide solely a perception change as well as interactions with virtual objects. Therefore, it can be applied in numerous areas such as education (providing interactive models to promote learning and training), medicine (training doctors and helping in diagnosing and treating patients), industry (equipment design or supporting maintenance operations) or entertainment (providing numerous games with different features and interactions) [36].

Although smart glasses and lenses are already being developed to provide AR experiences, they are still in early work, meaning that this technology still relies mainly on smartphones. This may constitute a constraint due to the small screen dimension which may limit object superimposition. Desensitization from reality, security issues and privacy problems also cannot be disregarded. Nonetheless, it is a concept with reduced limitations and ample social and economic advantages which are being explored exponentially fast in the current era [37].

1.3.3 VR/AR cueing applied to Hemispatial Neglect

Rehabilitation

Virtual Reality and AR are technologies that hold great promise for the assessment and enhancement of cognitive and spatial attention deficits. These concepts allow the user to repeatedly attend to and interact with stimuli presented in the affected side of space, stimulating the injured brain hemisphere [38]. Also, they allow all the interactions to be accurately quantified while capturing the patient's natural feedback (namely physiological signals) for posterior analysis. This provides for accurate and consistent assessment, therapy, and, ultimately, outcome measures. The head tracking attributes of the HMD make it very suitable for the evaluation of patients with hemispatial neglect as well as other visio-spatial disorders [29].

Thus, by utilizing VR/AR technology, different features of hemi-neglected patients can be assessed and measured. For example, their tendency to turn their head to the right (since the left side tends to be disregarded) in real world environments can be quantified to understand the extent of the underlying pathology. Additionally, also in a Virtual Environment provided by VR technology the patients tend to ignore the left side of their field of view. This tendency can be measured and ameliorated through VR application [29]. These types of measurements weren't present in the past and are only enabled by Virtual Reality, opening a new field in the non-intrusive rehabilitation of patients with HN.

The impacts of VR and AR cueing on improving the condition of HN victims is a concept that has started to emerge significantly in the 21st century. Although further research in required, a few studies report positive impacts on patients with this pathology and considerable transferability to the everyday lives of these improvements [29] [38].

An experiment conducted by Myers and Bierig [29] analyzed the impact of visual and auditory cues incorporated in a virtual environment, provided by VR technology. The right side of the FoV was patched, covering approximately 30% of this space. The participant was immersed in a three-room virtual house with a backyard and objects for the subject to interact (visual cues). Auditory cues were provided throughout the exercise. The flow of the layout of the rooms was biased to the left and moving objects (such as a virtual dog) move from the right to the left to influence the attention of the participant to the left (the injured side of the field of view) as much as possible. Afterwards, 3 different aspects of the patient's behavior were measured. First, the maximum angle of head rotation to the left and to the right. This phase tests and validates this VR application as a practicable tool to quantify and diagnose the extent of the pathology. Secondly, the time to reach the maximum angle in each direction was

measured. This second phase determines the effectiveness of the VR system in the improvement of left unilateral neglect. Finally, in the case of patients who ignore the left side, the number of cues the patient requires to turn to the left was also measured. This phase mainly measured cerebral metabolic activity using a PET. The results were positive and suggest that VR will be a viable diagnostic tool in the assessment of left hemineglect and overall neurorehabilitation. Nevertheless, it is important to notice the small sample of participants analyzed and, as such, even though the reports were promising, they constitute early work and further investigation is crucial.

A number of other experiments have supported the aforementioned positive impacts of VR cueing in patients with left HN but also the benefits of AR cueing. For instance, a study conducted by Smith et al. [38] assessed the impact of AR cueing on hemineglect through the application of the Behavioral Inattention Test (BIT) and the Bells Test before and after the virtual intervention. Although small, all four patients showed improvements in the different tests when comparing their performance before and after the intervention and in the follow-up (Figures 5, 6 and 7). The maximum possible score in the Bells Test is 35, in the BIT Behavioral Test it is 81 and finally, in the BIT Conventional Test it is 146.

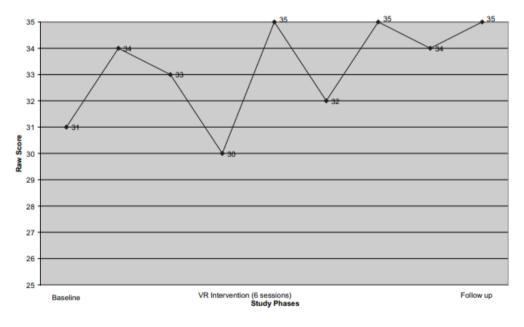


Figure 5: Participant Three's Bell Test Score.

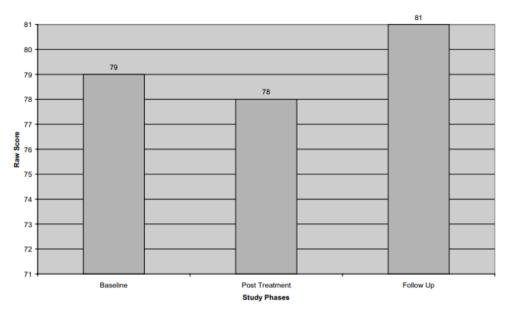


Figure 6: Participant Three's BIT Behavioral Subtest Scores.

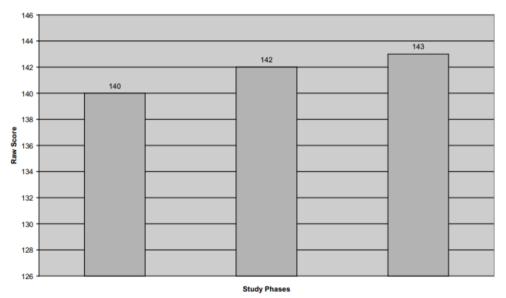


Figure 7: Participant Three's BIT Conventional Subtest Scores.

The AR intervention was composed of different virtual objects quickly passing through the actual FoV of the subject which was then asked to identify the correct objects (balls) while avoiding the wrong objects (birds).

After analyzing the results of this experiment before and after the intervention, an upwards trend can be identified, suggesting that the AR is, indeed, a viable tool for assessing and ameliorating the symptoms of left hemispatial neglect. Patients who underwent this experiment also reported reductions in their hemineglect in their everyday lives, namely in improved attention to their surroundings and, interestingly, conveyed satisfaction while performing the AR phase of the exam, which is a benefit unique to this type of intervention [38].

So, although VR and AR cueing are still in early works and further experiments and researches applied to a bigger sample are required, the advantages start to seem clear. With this recent type of

technology, numerous features that were previously merely theoretical can start to be applied. For instance, it enables the straightforward presentation of training scenarios that are difficult to present by other means, easy manipulation of the stimuli/cues to better adapt to each subject, the control and absolute consistency of training variables, the provision of different natures of cueing and the ability to incorporate the collection of physiological data and feedback tailored to each subject according to its impairment. Additionally, it decreases the therapist's involvement in AR-based rehabilitation techniques, reducing inherent subjectivity and providing a standardized therapeutic path. All these benefits allow for a personalized, effective, and patient-oriented therapy [29]. Additionally, numerous Augmented Reality and Virtual Reality applications and approaches are being explored. These include VR Cancellation Task, VR Line Bisection, VR Baking Tray Task (where the subject is presented with a tray with 16 identical cubes and is asked to spread them in a 4x4 formation, all equally separated), navigation through virtual environments while performing secondary tasks (such as naming all the objects present in the scene), pressing a response button when the desired object appears in a virtual environment, telling the time on a clock, maintaining the gaze on a given object, crossing a virtual street safely or grasping different objects [39].

However, the difficulties and limitations of this tool cannot be disregarded. In addition to the aforementioned limitations of physical cueing (which are also shared by VR/AR cueing), Virtual and Augmented Reality also have high inherent complexity and relatively high costs. Additionally, these systems can be complex to develop by anyone not trained in the area of software programming [29]. Nevertheless, these obstacles must be seen as challenges to overcome to ultimately increase the quality of life of everyone, namely hemispatial neglect victims, to the greatest extent possible.

1.4 Objectives and Proposed Approach

The goal of the present work is to develop a cross-modal intervention setup and methodology to not only simplify and standardize the rehabilitation practice of HN but also promote a quicker and more effective rehabilitation of individuals with the pathology. To achieve this, a strategy was designed considering an extensive bibliographic review performed regarding HN and the state-of-the-art in rehabilitation and therapy strategies. The main objective is to test the applicability, usability, and tolerability of this intervention, which aims to induce quick and solid improvements in the severity of the symptoms of the participants, allowing them to return to their normal condition. During the experiment, qualitative and quantitative data will be gathered to assess the applicability of the intervention plan. Data will also be gathered in order to inform about the robustness and validity of the strategy and whether changes should be made to support further studies in the area.

Due to the ongoing COVID-19 pandemic, the solution developed in this work will be tested on a preliminary group of healthy individuals to assess the applicability of the model, using different tools including AR. Testing on patients with HN in a clinical environment could compromise the safety of the patients since this solution would imply proximity between the researcher and the participant.

1.4.1 Novel Contributions

This experiment utilizes not only state-of-the-art technology as AR used in a way that has not been tested before but also combines it with auditory stimuli sequentially, which, up to the authors knowledge, is a cross-modal approach that has not yet been explored. Cross-modal approaches stimulate or demand different functional modalities of the subject (in this case, the visual and motor domains) and are known to have the potential of causing deep and long-term improvements. If the results are positive, in the future these tools may constitute a simple and intuitive solution with the potential to be used by healthcare professionals on bedside rehabilitation of patients or possible even daily by themselves to provide quick and direct improvements and increase autonomy.

1.5 Thesis Overview

The harm inherent to Hemispatial Neglect is clear. The impairment it brings to people's lives, accoupled with its high prevalence makes it a fundamental pathology to address. As aforementioned, the emergence of novel techniques such as Augmented Reality opens numerous doors regarding therapy pathways.

The work done by authors like Myers and Bierig [29], Smith et al. [38] or Hommel et al. [27] highlights the rehabilitation potential of such techniques. Using Augmented or Virtual Reality allows for an easy adjustment and consistency of cues provided leading to detailed, patient-oriented treatment strategies with the potential of causing long-lasting improvements in the visuo-spatial capabilities of the patient.

The previously mentioned research worked as a foundation for the current study. It is composed of 4 phases which will be further detailed in the following chapter. The first phase is composed of 4 exercises from the BIT – Line Bisection, Cancellation Task, Clock Test and Article Reading. The second phase consists of a cross-modal approach using visual and auditory cues. To achieve this, the author developed two AR games to provide visual cues and two auditory games to provide auditory cues. The AR games were developed using C# programming language in the Unity platform [40]. The auditory games were developed using the Adobe Premiere software [41]. These exercises stimulated different aspects of the participant, namely their visual and motor capabilities. In the third phase, the participants performed the same exercises of the phase 1 to assess improvements and the pertinence of the strategy and in phase 4 each participant filled out the Game Experience Questionnaire [42] to assess the applicability and validate the solution.

Data was gathered throughout the whole intervention which will also be discussed ahead. Finally, numerous conclusions were drawn from the results and compared to previous work done in the area by other authors. To substantiate further work based on this research, a few improvements are also pointed out in the end of the dissertation.

2. Methodology and Experimental Setup

This chapter is focused on the detailed explanation and thorough description of the strategy applied to the preliminary group of participants. This intervention plan was analyzed and validated by Dr. Pedro Nascimento Alves, Department of Neurosciences and Mental Health, Neurology, Hospital de Santa Maria, who accompanied the development of this solution. It is composed of 4 distinct phases: the first phase included preliminary tasks to assess the extent of the neglect, any important particularities of the subject that should be taken into account and to provide a straightforward method to analyze the benefits and applicability of the plan by comparing the answers before and after the second phase; the second phase comprised visual cueing using AR and auditory cueing to stimulate the spatial attention, motor activation and accuracy of the subject; in the third phase, the subject was asked to repeat the tasks performed in first phase with a few variations in order to identify possible improvements, their significance and the applicability of the solution; finally, in the fourth phase the participant was presented with a version of the Game Experience Questionnaire (GEQ) [42] to quantitively assess the game experience. The tasks were all performed in the same session. Additionally, the extension of the treatment plan was designed to be as wide-ranging as possible while not causing the subject to feel fatigued and to feel comfortable. The tasks in the first and third phases were performed via pen and paper.

Nine participants contributed to this experiment (mean age = 30.8 years, standard deviation = 13.3 years, age range from 23 to 54 years). None of these participants had any pre-existing visuo-spatial pathologies which could directly impact the tasks at hand, or any diseases that could have caused lack of collaboration of cognitive incapacities. Seven of the nine participants were right-handed and two were left-handed. The place in which the participants performed the tasks was different between participants due to their different locations (which can be visualized in Figure 8), but it was assured that the settings were similar, without distractions and a clear FoV when performing the AR tasks. The participants seated across the researcher and were clearly instructed in how to perform each task. They were presented with a blue pen to carry out the pen and paper tasks. It is important to notice that the size of the sample was influenced by the ongoing COVID-19 pandemic, which highly limited the ability to travel and, since this experiment does not allow social distancing in certain tasks (namely the VR and auditory cueing exercises, which require the researcher to place the HMD on the participant), and even though all sanitary measures were followed, it was preferred to keep the sample size reduced to avoid any possible infections.



Figure 8: Locations where the solution was applied, and the results were obtained (map created with Microsoft Power BI [60]).

2.1 Phase 1 – Preliminary Tasks

In the first phase, the subject was asked to complete 4 tests from the Behavioral Inattention Test battery. The participant performed 2 tests from the BIT Conventional subtest – Line Bisection and Task Cancellation – and 2 tests from the BIT Behavioral subtest – Clock Test (modification of Telling and Setting the Time and Picture Drawing) and Article Reading [43] with a few modifications which will be detailed ahead. These tests addressed the most common and significative symptoms of Hemispatial Neglect – spatial and motor neglect.

2.1.1 Line Bisection

The Line Bisection (LB) test is a widely used, fairly efficient task to assess the presence and severity of Hemispatial Neglect. It provides a straightforward method of comparison between before and after the intervention. In this test, the patient was presented with a sheet of paper including 3 horizontal lines, 1 closer to the left, 1 at the center and 1 closer to the right in a staircase fashion with a length of approximately 8 cm (see <u>Appendix A</u>). The subject was then asked to mark the middle point of these lines with a blue pen. This task has an expected duration of 1 minute.

2.1.2 Cancellation Task

The Cancellation Task (TC) test is, as the LB test, an efficient method to evaluate the degree of impairment of the subject while providing a direct way of comparison between before and after the intervention. The patient was presented with a sheet of paper at its midline with multiple distractors and

was asked to scan it to locate and identify 2 specific objects – a black and a white circle. The target objects were presented in the sheet of paper with two different sizes (large and small) among the distractors and the patient was asked to identify the objects, regardless of their size. A first sheet with fewer objects and one of them identified was presented as a demonstration to aid the subject in performing the task proficiently. It was assured that the wanted objects were presented in the left, center, and right sides of the sheet. The objects were all, approximately, evenly spaced with 0.8 cm between them, spread across 22 columns and 17 lines and all either black and/or white. There were 48 targets objects and 326 distractors (see <u>Appendix A</u>). This task has an expected duration of approximately 5 minutes.

2.1.3 Clock Test

The Clock Test is a variation of the Telling and Setting the Time task from the BIT battery. It encompasses two distinct phases. Initially, the patient was presented with a sheet which contained a clock with a given hour (with a pointer in the left side of the clock and a pointer in the right side) (see <u>Appendix A</u>). The patient was then asked to verbally say the exact hour presented on the clock. Afterwards, the patient was tasked to copy this image to another sheet of paper as accurately as possible. This task had an approximate duration of 3 minutes.

2.1.4 Article Reading

The Article Reading task allows the assessment of visuospatial dysfunctions independently, since it requires no motor function. The patient was presented with a sheet of paper with a text divided in 3 columns (left, center and right) (see <u>Appendix A</u>). The patient was then asked to read the text. There was an effort to keep the size and complexity of the words homogeneous throughout the different columns. This task has an expected duration of approximately 1 to 2 minutes.

The tasks chosen for the first phase of the intervention plan considered a few details. Although some adjustments were made to better adapt to the strategy, the tasks were selected from the BIT battery – a commonly used tool for Hemineglect diagnostic and assessment. Also, in the Task Cancellation test, the patient was asked to scan and locate, in a sheet of paper, 2 target objects, which only changed in color and appeared in different sizes. This allows for the detection of patterns or biases based on the performance of the participant (size and color prioritization), which could prove useful in the diagnosis and assessment of hemispatial neglect.

Furthermore, it is also important to notice that the first two tasks (LB and TC) do not inform about motor and spatial dysfunctions independently since the patient utilizes both spatial capabilities (scanning the sheet of paper) and motor skills (to either mark the middle point of the line or identify wanted objects) – by understanding where the issue lies (spatial or motor), the results of the intervention can be interpreted differently. To tackle this issue, the final two tasks from the BIT Behavioral subtest address the two types of neglect in a dissociated way. The first part of the Clock Test (telling the time) requires spatial skills exclusively while the second part (copying) also includes motor activation – this provides

data to inform about significant neglect characteristics. The final task (Article Reading), similarly, only demands spatial attention to corroborate previous inferences. Finally, the different tasks were presented to the patient via pen and paper because, on the one hand, this is the standard procedure when applying tests from the BIT battery and, on the other hand, the vast majority of the previous experiments conducted in the field also applied these tests via pen and paper and so, in order to be able to directly compare the results, the tests should be applied under similar conditions.

Thus, the author considered that these 4 tests in the first phase of the intervention plan were the optimal approach, as the duration was not overwhelming while covering every important aspect of the patient's condition.

2.2 Phase 2 – Virtual and Auditory Cueing

The phase 2 of the rehabilitation plan can be considered the intervention itself. It included the exercises to stimulate spatial and motor skills of the participant in order to cause positive, long-lasting changes in its condition. It encompassed 2 sub-phases: first, the participant underwent a visual cueing AR game and afterwards 2 tasks which involved auditory cueing.

2.2.1 Visual Cues

The visual cues were provided to the participants using Augmented Reality presented on a *Samsung Galaxy A70* [44]. Both the phone and the Virtual Reality HMD were provided by NEVARO [45]. The author developed the mobile applications where the Augmented Reality cues were presented using the C# programming language in the Unity platform – a cross-platform game engine used to create AR, VR, simulations or other game experiences in an accessible way [40]. The applications were inspired by the aforementioned bibliographic review, namely the works of Myers and Bierig [29], Smith et al. [38] and Hommel et al. [27] and also suggestions and advices provided by Dr. Pedro Alves.

The first game consisted in flashes of 2 red spheres (exemplified in Figure 9) in the upper part of the FoV – 1 in the left side of the FoV and 1 in the right side. The application flashed the spheres unilaterally or bilaterally, which means that the patient saw either 1 sphere in 1 side of the FoV or both spheres simultaneously. The symmetry between the position of both flashes was maintained throughout the task. The time intervals between the flashes was 1 second. The flash duration was also 1 second. The flashes of the spheres started in a position closer to the center and, as the time progressed, they moved towards the periphery of the field of view, assuming 3 different symmetrical positions. The subject was tasked to identify verbally the position of the flashes as they appeared by saying "esquerda" - left, "direita" - right or "ambos" – both. The answer was registered as right or wrong by the researcher at the same time the participant is providing the answers by using tables containing all the stimulus, their cadence and time intervals, which will be explained the <u>Data Collection and Analysis</u> subsection. A shorter version of this application was developed to be presented to the patient for practicing, prior to the exercise itself. This exam has an approximate duration of 3 minutes, excluding the practicing phase. This practicing demonstration was developed to familiarize the participant with the requirements and demands of the application and reduce errors not due to the pathology of HN.

The second game (exemplified in Figure 10) consisted of 3 different 3D shapes appearing in random parts of the FoV of patient, who was then asked to identify which shape appeared. The shapes were spheres, cubes, and cylinders. The shapes appeared in 6 different positions which focused mainly on the left side of the FoV. Each cue appeared for 1 second and the interval between cues was also 1 second. Only one shape was presented at a time. The participant was then asked to verbally identify which shape appeared by saying "cubo" - cube, "esfera" - sphere or "cilindro" – cylinder. Like in the previous task, a shorter version of this application was developed to be presented to the patient prior to the task for practicing and the answer was registered as right or wrong by the researcher at the same time the participant is providing the answers by using tables containing all the stimulus, their cadence and time intervals, further explained in the <u>Data Collection and Analysis</u> subsection. The duration of this exam was approximately 3 minutes, excluding training.



Figure 9: Demonstration of the first AR game – the red spheres flash uni or bilaterally, to be identified by the participant, and move towards the periphery over time. The bottom cue serves as support to help understand the purpose of the game.



Figure 10: Demonstration of the second AR game – the different shapes flash sequentially in random areas of the FoV, to be identified by the participant. The bottom cue serves as support to help understand the purpose of the game.

2.2.2 Auditory Cues

The auditory cueing phase encompassed two distinct tasks. Both were provided to the patient using a *Samsung Galaxy A70* and its associated earphones [44] provided by the startup company NEVARO [45]. The auditory cueing games were developed using the Adobe Premiere software [41]. The sounds were monophonic and had an audio bit depth of 16 bit. Once again, these tasks were based on both the bibliographic review performed prior to the design of this intervention plan and feedback from Dr. Pedro Alves. As in the visual cueing tasks, the answers provided by the participants were registered as right or wrong by the researcher, live, by using tables containing all the stimulus, their cadence and time intervals, explained in the <u>Data Collection and Analysis</u> subsection.

The auditory cues were simple beep sounds. The volume of the auditory cues was adjusted as to not cause any type of discomfort on the subject. In the first task, the subject was presented with auditory stimuli appearing in either the left ear channel, the right ear channel or in both channels simultaneously. The stimuli had a consistence cadence of 3 seconds between each cue. The cues lasted for 0.6 seconds. The subject was asked to verbally identify in which ear channel the cues appeared. In the second task, the subject was presented with bilateral auditory cues. These cues had random time intervals between them which were defined prior to the experiment (these time intervals were either 1, 2 or 3 seconds). These cues also lasted for 0.6 seconds. The subject was tasked to identify the cues every time they appeared by raising the hand of their unaffected upper limb (right).

2.2.3 Outline of Phase 2

The outline of the second phase accounts for important details. First of all, it is important to note that the AR applications were developed for the Android operative system and, thus, any Android smartphone is able to run the applications. Moreover, this facilitates the distribution of this solution in the future, since it does not require expensive AR/VR equipment and works with, for example, cardboard goggles. The goggles used, shown in figure 11, allow for the insertion of the smartphone laterally.



Figure 11: Goggles used for the AR tasks.

Regarding the stimulus, red spheres were chosen due to their higher contrast with real-world backgrounds – the color red is usually associated with danger or threat and so, draws attention more effectively. The geometry of the objects (sphere, cube, and cylinder) was chosen to also contrast with the background, since it is not a common form to appear in the upper part of the FoV, and also because they are simple forms, easy to identify by the participant.

Furthermore, AR technology was chosen to perform this task instead of Virtual Reality since it has been shown in previous studies that using visual cue superimposition in the real environment provides better results and higher transferability to the everyday lives of the patients [39]. Also, by using AR instead of VR, it is possible for the patient to, in a possible future, use it in its quotidian with more ease (at home, outside or even at work) since it does not significantly alter the subject's perception of the real world, providing a quick and simple method to ameliorate hemineglect symptoms – there is a smoother scalability between the clinical environment and the patient's day-to-day by using AR.

Additionally, the first visual cueing test using AR takes advantage of gradients. The red sphere flashes start off in a near-central position and move towards the periphery of the FoV over time. This allows not only to more accurately identify where the key dysfunction lies, but also to compel the subject to direct the attention to the more lesioned areas of the field of view.

Regarding the auditory exercises, it should be noted that the first exercise has consistent time intervals between cues since the attention of the subject should be directed to which ear channel was activated rather than when it was activated (*where* rather than *when*). In the second exercise, the time intervals vary throughout because the subject should not recognize any patterns and try to raise the right arm as quickly as possible after the cue appears (*when* rather than *where*) – this is believed to increase motor activation capability while improving spatial attention.

Furthermore, neither of the first two exercises (AR test and first auditory test) promote motor activation. Thus, the second auditory test complements the prior exercises, by demanding motor skills, originating a comprehensive, cross-modal intervention plan which stimulates different domains of the subject. It is also important to note that the motor activation exercise is provided via auditory cueing and not via Augmented Reality because, to provide new knowledge, an effective motor exercise using AR technology must include recognition of the hands of the subject and, up to the author's knowledge, hand recognition using mobile phone cameras is still an area under development and its implementation is still under-optimized and computationally intensive. Thus, the auditory task was preferred.

By utilizing visual cueing exercises, auditory exercises and limb activation, a cross-modal intervention plan was constructed which is believed to cause positive and long-lasting improvements on the HN symptoms of the patient.

2.3 Phase 3 – Task Repetition

In this phase, the subjects were asked to repeat the tests from phase 1 with some adjustments to collect data for posterior analysis regarding the impact of the intervention plan.

First, the Line Bisection Test was repeated under the same conditions as phase 1 (see <u>Appendix</u> <u>B</u>).

Then, the Task Cancellation was also issued. However, in order to not allow the subjects to recognize any patterns or recall the position of the wanted objects from memory which could bias the results, 2 different wanted objects were requested (black and white stars of any size). It was assured that in both phase 1 and 3 the wanted object was present on both sides of the sheet. There were 38 target objects in this new phase and 336 distractors (see <u>Appendix B</u>). It is also important to notice that the Bells Test from the BIT was not used since it was necessary to apply the Cancellation Task twice, in phase 1 and phase 3. Thus, and since the participants are asked to search for different targets in both phases, the Bells Test couldn't be used, and a different image was selected.

The Clock Test was performed once again. In this phase, the clock presented a different hour while maintaining a pointer in each side of the clock (see <u>Appendix B</u>).

Finally, the Article Reading exercise was performed again using a different article of text. The text was, as before, divided in 3 evenly separated columns (see <u>Appendix B</u>). In both phases, the articles were obtained from *Infoescola* [46].

2.4 Game Experience Questionnaire

After the 3 phases described above, the participants were presented with the first and third modules of the Game Experience Questionnaire (GEQ) [42]. The second module was not applicable in this experiment since it measures Social Presence. The questionnaire was presented in English and translated or explained whenever the participant requested so.

The first module is the Core Module or Core Questionnaire. It assesses the game experience quantitively on seven components: Immersion, Flow, Competence, Positive and Negative Affect, Tension, and Challenge. It is composed of 33 items (see <u>Appendix C</u>).

The third module of the GEQ is the Post-Game module. It assesses the participant's experience after the experience ends on four components: Positive Experience, Negative Experience, Tiredness and Returning to Reality. It is composed of 17 items. (see <u>Appendix C</u>)

2.5 Data Collection and Analysis

In phases 1 and 3, data was collected for analysis. This data allowed to understand the severity of the pathology, the main symptoms, and the impact of the intervention plan on the condition of the subject.

In phase 1, the data from all 4 tasks was recorded in a results sheet – see Appendix C.

- In the Line Bisection test, the distance from the subject's bisection to the actual midpoint was collected. Deviations to the left were registered as negative and deviations to the right were registered as positive. The results before and after the intervention were analyzed.
- In the Task Cancellation, the number of identified wanted objects, whether the size of the object
 had any type of impact on the performance and the omissions in the upper and lower halves of
 the sheet were identified.
- In the Clock Test, it was registered if the patient correctly identified the time presented on the clock and the subsequent copy was collected for posterior comparison and analysis.
- In the Article Reading test, the number of words omitted by the patient was recorded.

In phase 2, data was also gathered for statistical purposes. The number of correctly identified visual cues in the first and second tests, the number of correctly identified auditory channels from auditory cues in the third test and the number of identified cues in the fourth test were registered. This data was registered in the Results sheet, which had different tables for each test corresponding to the different cues, their cadence and time intervals (see <u>Appendix C</u>).

In phase 3, the process of phase 1 was repeated and the same data was collected, also in the results sheet.

It is also important to acknowledge that the process with which the patient performed the tasks was considered - where the scanning process began and whether it was methodical or unmethodical. Qualitative comments were also gathered regarding the subject's performance in order to obtain a more detailed and thorough analysis of the results.

Regarding the GEQ, in all items from both modules, the participant was asked to score each item with a number from 0 (totally disagree) to 4 (totally agree). In the first module, the Core module, each of the 33 items was associated with one of the seven components. The score for each component was obtained by computing the average of all the correspondent items. A similar process was conducted in the Post-Game module, where each of the 17 items was associated with one of the four components. The score for each component in both modules was obtained by computing the average of all the correspondent items.

In the Core module, the 7 components were associated with the 33 different items using the following method:

Competence: Items 2, 10, 15, 17, and 21. Sensory and Imaginative Immersion: Items 3, 12, 18, 19, 27, and 30. Flow: Items 5, 13, 25, 28, and 31. Tension/Annoyance: Items 22, 24, and 29. Challenge: Items 11, 23, 26, 32, and 33. Negative affect: Items 7, 8, 9, and 16. Positive affect: Items 1, 4, 6, 14, and 20.

In the Post-Game module, the 4 components were associated with the 17 different items using the following method:

Positive Experience: Items 1, 5, 7, 8, 12, 16 **Negative experience**: Items 2, 4, 6, 11, 14, 15. **Tiredness**: Items 10, 13. **Returning to Reality**: Items 3, 9, and 17.

Therefore, a comprehensive, cross-modal strategy is employed. The GEQ, applied at the end of the intervention, will elucidate about its quality, its weaker and stronger points, and the possible improvements to be implemented before clinical application.

It is also important to note that, prior to the experiment, all participants were provided a written informed consent (detailing the outline of the strategy and its expected benefits and weaknesses) and an informative sheet (answering general questions regarding the experiment) (see <u>Appendix D</u>).

3. Results

In this chapter, the results obtained in the different phases of the experiment will be presented, which were registered in the results sheet. As previously described, the different tasks extracted from the BIT battery were performed before and after the cross-modal intervention in order to identify improvements and the applicability and validation of the strategy. At the end of the intervention (pen and paper tasks followed by exercises based on AR and Auditory stimulus and, lastly, repetition of the pen and paper tasks), the participants were asked to fill out the Game Experience Questionnaire to rate their Augmented Reality experience. The results of the 9 participants will now be presented.

3.1 Line Bisection

The results obtained for the 9 participants in the Line Bisection task are now presented. The errors were measured with a ruler and are presented in millimeters.

Participant	Le	ft	Cen	ter	Rig	Right	
Purticipunt	Before	After	Before	After	Before	After	
Р.В.	-2	0	0	0	0	0	
M.F.	0	1	-5	1	1	1	
L.P.	3	0	2	0	3	1	
M.P.	0	-3	0	1	2	1	
B.G.	0	1	-1	0	0	-1	
M.R.E.	1	0	0	0	-2	0	
J.C.B.	1	0	1	0	1	-1	
J.B.	0	0	0	0	0	0	
<i>R.B.</i>	0	0	-1	0	-1	0	
Median	0	0	1	0	1	1	
Interquartile Range	1.5	1	1.5	0.5	2	1	

Table 1: Results obtained from the Line Bisection Test for each participant (in millimeters) before and after phase 2.

The results show the distance to the middle point of the line, where positive values represent a deviation towards the right and negative values represent a deviation towards the left. It is important to note that the participants did not display any type of adverse or hostile reaction while carrying out this task and, instead, completed it comfortably. Moreover, they completed this task in well under one minute.

To perform a statistical analysis of the results for the whole set of results regarding the lines in the left, right and center (theoretical value is 0; N is the number of participants):

$$Percent\ error = \frac{\sum \frac{experimental\ value\ -\ theoretical\ value\ }{1\ +\ theoretical\ value\ }}{N} \ x\ 100\ = 7.2\%$$

The median and interquartile range show a reduced error and variability throughout the 3 lines. The median of the results is reduced (either 0 or 1 millimeters – since the lines were 8 cm long, 1 millimeter corresponds to 1.25%). Furthermore, the interquartile range shows the small variability of the results – highest variability is observed in the right line before phase 2, where the interquartile range is 2 millimeters, corresponding to 2.5% of the total length of the line. All the participants carried out this task effortlessly and their answers never presented any significative deviation from the middle point of the different lines (total error rate of 7.2%). It is also observable that, even though the participants did not have any type of visuospatial pathology and the errors are residual, the results in the Line Bisection task were significantly better after the intervention in the three lines, with improvements as high as 80% (which occurred in the center line).

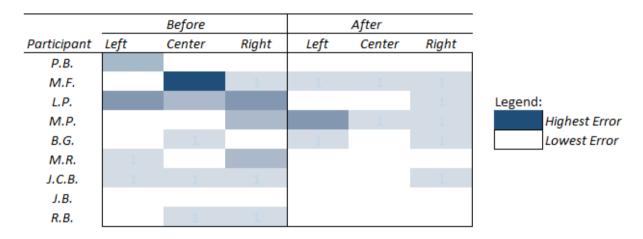


Figure 12: Heat Map representing the absolute error distribution before and after phase 2.

3.2 Task Cancellation

The results obtained for the 9 participants in the Task Cancellation are now presented.

Participant -	Identifi	cations	Omissior	ns Before	Omissions After		
Purticipunt	Before	After	Upper	Lower	Upper	Lower	
Р.В.	46/48	36/38	0	2	0	2	
M.F.	47/48	37/38	1	0	0	1	
L.P.	48/48	33/38	0	0	1	4	
M.P.	47/48	38/38	1	0	0	0	
B.G.	47/48	33/38	1	0	1	4	
M.R.E.	48/48	38/38	0	0	0	0	
J.C.B.	47/48	37/38	1	0	0	1	
J.B.	48/48	38/38	0	0	0	0	
<i>R.B.</i>	47/48	38/38	1	0	0	0	
Percentage Error (%)	1.63	4.11					

Table 2: Results obtained from the Task Cancellation for each participant before and after phase 2.

The results show the number of identifications, with the respective percentage error and omissions in the upper and lower halves of the exercise. In this case, the number of omitted objects in the upper and lower half of the image is shown instead of the right and left halves because the participants do not have any visuo-spatial pathologies and, thus, it is expected that no patterns will occur in the omitted objects between the right and left halves of the image, corroborated by, for example, the work of Warren et al. [47] where healthy subjects presented error rates under 4% and no patterns regarding left and right omissions. It was observed that the number of objects missed in the TC of phase 3 was higher and should be discussed. The participants completed this task in, approximately, 5 to 7 minutes.

Throughout this task, there weren't any observable adverse reactions and the participants completed the task with ease.

To perform a statistical analysis of the number of identified targets (theoretical value is 48 for the first column of data and 38 for the second which corresponds to finding all objects; N is the number of participants; μ is the mean of the dataset):

$$Percent \ error \ before = \frac{\sum \frac{experimental \ value - theoretical \ value}{heoretical \ value}}{N} x \ 100 \ = 1,6\%$$

$$Percent \ error \ after = \frac{\sum \frac{experimental \ value - theoretical \ value}{heoretical \ value}}{N} x \ 100 \ = 4.1\%$$

$$Standard \ Deviation \ before \ \sigma_1 = \sqrt{\frac{(\sum |x-\mu|^2)}{N}} = 0.6$$

$$Standard \ Deviation \ after \ \sigma_2 = \sqrt{\frac{(\sum |x-\mu|^2)}{N}} = 2,0$$

The error for phases 1 and 3 is 1.6% and 4.1%, respectively. In the first phase, the average number of identified objects is 47.2 ± 0.6 and in the second phase it is 36.4 ± 2.0 . The standard deviation is considerably higher in the second phase when compared to the first – this is observed in the lower part of the Task Cancellation test applied after the intervention, where the number of omitted targets increased substantially (more than half the participants had at least 1 omission and the average number of omissions is the largest of the four analyzed halves). Finally, it is also worth noting that, when analyzing the impact of the color of the target on the performance of the participants, no patterns were identified since the error is extremely low and when there were omissions, the black and white targets were omitted similarly – of all the omissions, approximately 48% corresponded to omissions of white targets and 52% to black targets. However, regarding size, 43% of all omissions corresponded to large targets and 57% to small targets – a greater difference when compared to the impact of color on the performance.

3.3 Clock Test

The participants were able to perform the Clock Test without difficulty, as expected. They were able to correctly identify the time presented and draw an analogous clock without any type of significative asymmetries or omissions.

Most importantly, during this task, the participants did not show any type of discomfort or adverse reactions to the exercise. This exercise was completed in around 2 minutes.

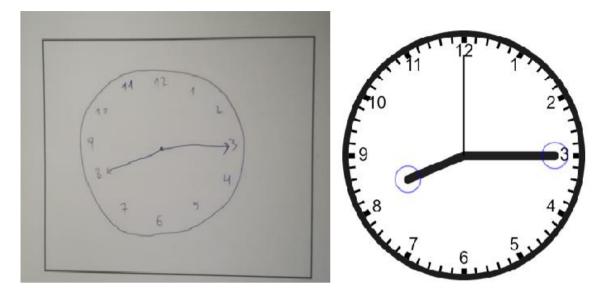


Figure 13: Clock drawn by one of the participants (J.B.) compared to the actual clock presented.

3.4 Article Reading

Similar to the Clock Test, and also as expected, the participants were able to complete the Article Reading task easily, reading the excerpt without difficulty. Also, this task did not cause any type of unexpected reaction in the participants, who accomplished it comfortably, taking roughly 1 to 2 minutes to complete it.

3.5 Phase 2

The performance of the participants in the AR and auditory tasks was also quantitively measured. By using tables present in the Results sheet (<u>Appendix C</u>) containing references of the stimulus used in the different exercises, it was possible to verify the veracity of the participant's answers in the different tasks. After the data was collected for every participant, it is possible to ascertain that all participants were able to complete the tasks without difficulty and provided the correct answers in every task, as it was expected. Furthermore, the participants clearly expressed satisfaction and ease when performing the AR tasks. After the AR and auditory tasks, the participants were asked whether they thought the cadence of the exercises was suitable and all the answers were positive. The exercises had a duration of 2 minutes each. After the exercise was explained to the participants, they were asked if they wanted to practice, prior to the exercise itself, using a training application which consisted of a shorter version of the main application, with a different cadence of stimuli. The participants that requested training had an approximately 30 seconds long practice session using the training application. The training phase was not applied to all participants because they showed clear understanding of the requirements of the task – furthermore, the results showed that the training did not have an impact on the performance of the participant, since all participants correctly identified all cues.

3.6 Game Experience Questionnaire

The results for the GEQ are now presented (maximum score of 4 and minimum score of 0).

Participant	Competence	Positive Affect	Flow	Sensitive and Imaginative Immersion	Challenge	Negative Affect	Tension/ Annoyance
P.B.	3.6	3.8	2.6	2	0,6	0.3	0
M.F.	4	3.8	2.6	2.2	0.8	0.3	0
L.P.	4	3.4	2.4	2.2	0.6	0.3	0
M.P.	4	3.8	3.6	2.3	0	0	0
B.G.	3.4	4	1.6	3.2	0.4	0.5	0
M.R.E.	4	3.6	2.8	2.3	0	0	0
J.C.B.	4	3.4	2.8	1.3	0	0	0
J.B.	3.6	3	2.4	2.8	1.6	0.5	0
R.B.	4	3.6	2.6	1.8	0.6	0	0
Average	3.8	3.6	2.6	2.2	0.5	0.2	0

Table 3: Results obtained from the Core module of the Game Experience Questionnaire

Table 4: Results obtained from the Post-Game Module of the Game Experience Questionnaire.

Participant	Positive Experience	Negative Experience	Tiredness	Difficulty Returning to Reality
P.B.	2	0	0	0
M.F.	2	0	0	0
L.P.	1.8	0	0	0.3
M.P.	3.5	0	0	1
B.G.	2.2	0.2	0	0
M.R.E.	0.3	0.3	0	0
J.C.B.	0.7	0	0	0
J.B.	1	0	0	0.7
R.B.	2	0	0	0.3
Average	1.7	0.1	0	0.3

The results show the scores obtained in each item of the Core and Post-Game modules of the Game Experience Questionnaire. This questionnaire is filled based solely on the Augmented Reality experience, without accounting for the remaining tasks. The minimum score was 0 and the maximum score was 4 in every item. The Core module refers to the in-game experience while the Post-Game module concerns the experience after the game is finished. In both cases, it is observed that the participants rated the solution as positive, and causing no annoyance, tension, tiredness, or difficulty returning to reality. During the AR games, the participants rated the sensitive and imaginative immersion and flow as 2.2 and 2.6 out of 4, respectively.

Score for each component in the GEQ

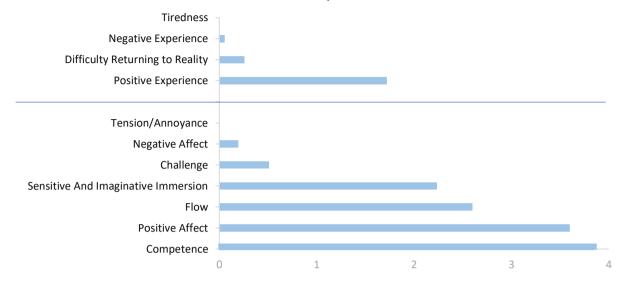


Figure 14: Scores for each component in the Game Experience Questionnaire [42] (the upper part presents the scores for the Post-Game Module; the lower part contains the scores for the Core Module).

Three participants claimed that the immersion of the solution was compromised due to the HMD – it put too much pressure on the nose, causing discomfort. These participants held the glasses with their hands to relieve some of this pressure while performing the tasks. Also, they stated that the glasses defocused that game slightly.

Finally, it should be noted that, after performing each task, all participants were asked orally how they felt while and after performing the exercises, if the exercises were intuitive, if they caused any type of discomfort or if the flow of the strategy was suitable. The responses were all positive excluding the aforementioned statements about the HMD in the AR tasks and 2 participants who claimed that the duration of the Task Cancellation was rather long.

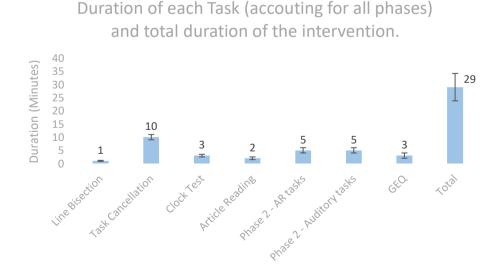


Figure 15: Duration of each task, in minutes. The duration of the Line Bisection, Task Cancellation, Clock Test and Article Reading in the graph show the sum of their duration in phase 1 and 3.

4. Discussion

In this chapter, the results of the experiment will be analyzed, discussed, and compared with existing clinical and experimental data obtained by other authors.

First of all, it is important to remark that the format and elements of the intervention were designed to be applied to HN patients and, as such, participants without any type of visuospatial pathologies will be able to complete every task without difficulty. The target group of this solution are people over 65 years old [48], which is the age group more prone to stroke and, thus, the main goal of the intervention is to stimulate the spatial attention and muscular activation of the participant through simple, non-invasive tasks, while using a cross-modal strategy, believed to cause longer-lasting improvements. It was not possible to test this solution with individuals within that age group mainly due to the ongoing pandemic, its inherent travelling restrictions, and the fact that people over 65 years old constitute the higher risk group of COVID-19.

When testing this solution on healthy participants, the results obtained are expected to be nearly flawless, with residual errors. Nonetheless, this phase of the research – experimenting the solution on healthy subjects – is fundamental prior to the clinical practice since it not only allow the assessment of the applicability of the solution but also highlight the stronger points of this solution and their benefits, its weaker points (to be adapted or removed) and their repercussions, indicate the improvements to be implemented, and whether it is applicable to Hemispatial Neglect patients at all. More important than the quantitative analysis of the results obtained, this research phase is important due to the qualitative analysis it allows – understanding if the participants perform the different tasks comfortably, if the flow of the intervention plan is applicable, if the cadence of the exercises is suitable, if any of the exercises is too easy or too hard or if the solution triggers any type of unforeseen reaction in the participant. All these conclusions allow the adjustment of the whole strategy so the clinical practice can be as effective and enriching as possible.

The results of each task will, initially, be analyzed independently:

Line Bisection: the errors committed by the participants were very low, as it was expected. The participants completed the exercise effortlessly and no adverse reaction was observed or expressed. Regarding the results, it is important to notice that, even though the errors are residual, there is an improvement of the results when compared before and after phase 2, which is clear in the <u>Heat Map</u>. There are 2 possible justifications for this improvement: it could be argued that this cross-modal intervention plan is, in fact, effective in increasing the spatial attention of the participant, even if it is completely healthy, lacking any visuo-spatial pathology. The second justification lies on the fact that, even though there are improvements, the errors are still extremely low in both phases and the participant sample is reduced. Thus, the worse results in the first phase could be due to accidental errors, which can be caused by a number of factors (lack of attention, nervousness, etc.) and are relatively common. The learning factor (participants learning how to perform the task in the first phase and consequently having a better performance in the second application of the exercise) can also play a part in the

performance improvement. This should be considered when applying the solution to and analyzing the performance of Hemispatial Neglect patients – small errors may be due to factors other than the pathology itself. In the clinical practice, the results obtained from HN patients are expected to have larger deviations to the right, especially the line on the left, which is the side of the FoV that tends to be affected in hemineglect. The phase 2 of the intervention (AR and auditory tasks) is expected to have an ameliorating effect on the participant and, thus, the results from the second time the Line Bisection task is performed (phase 3) are expected to be improved. Due to the reduced percentage error displayed in this exercise, it is also concludable that the difficulty is suitable.

The results obtained are corroborated by previous work done in the field. A study conducted by Julia Van Deusen tested the performance of 93 non-brain damaged elderly participants on the Line Bisection test [49]. Even though the mean age of the sample in the study was significantly higher than the mean age of the current study (70.5 and 30.8 years, respectively), the results showed that the mean error is close to zero (deviation of 0.48 ± 5.55 mm for the left lines and 0.59 ± 4.35 millimeters for left plus center lines) – this allows the extrapolation that in the current study, the error should also be near zero (which, in fact, is observed), since the visuo-spatial capabilities tend to deteriorate with age. A similar, more recent research done by Gamberini et al. analyzed the impact of the distance between the participant and the line in the Line Bisection test on healthy participants. The experiment concluded that the error increases with distance but is also always near zero – for the different distances experimented (30, 60, 90 and 120 cm), the mean deviation was never larger than 1.03 mm [50]. Thus, the results obtained in the current study are in agreement with experiments previously conducted in the area.

Task Cancellation: Once again, the results were very low in both phases and the participants accomplished this task with ease, although 2 participants claimed that the duration of these exercises was fairly long. The results are notably worse in the second phase, namely in the lower half, with a slightly larger error and larger standard deviation. It was also observed that the participants perform this task with a standardized method of scanning, prioritizing left to right and then top to bottom. Thus, in the upper halves of the Task Cancellation performed in phase 1 and 3, the error rate is lower. However, in the lower half of the Task Cancellation in phase 3, the number of omissions is higher which does not happen in phase 1 (error rate increases from 1.6% to 4.1%). Since the participants use a method of scanning which prioritizes the upper half and the errors occur in the lower half in phase 3, there are a few possible justifications: the duration of the intervention plan is too long, causing the participants to feel weary when performing this exercise (it was claimed by 2 participants that the duration of these Cancellation Tasks was rather extended); the exercise of the Task Cancellation in phase 3 is harder than the Task Cancellation in phase 1 (since the increase in the error percentage only happens in phase 3) which was not designed as such; the difficulty in sustaining attention for long periods of time in repetitive scanning exercises (the factor of fatigue can have a large impact in this task since it is applied after phase 1 and 2). Finally, and since the participant sample is reduced, similarly to the Line Bisection task, it could be argued that the rise in the omission rate in the lower half of phase 3 is due to accidental errors because the percent error is minor in both phases. Nonetheless, this error increase should be considered prior to clinical application - to counteract it, the size of these exercises should be shortened.

It is also important to notice that the omissions regarding size presented a higher discrepancy than regarding color (where both colors were omitted similarly) – 57% of all omissions corresponded to smaller objects. This can be justified by the higher difficulty of identifying smaller objects, which is held true even to healthy individuals. This should also be considered when analyzing the results obtained from HN patients – a higher rate of omissions of smaller objects may not only be due to the HN but also to the aforementioned difficulty and thus, the results should be compared to those of healthy subjects to evaluate the contributions of both causes and obtain a broader idea of the pathology. Furthermore, larger objects also provide high significance, since a larger rate of omissions of this type of targets may help diagnose and assess the condition of the patient.

In a clinical setting, when applying this solution to HN patients, it is expected that the number of omissions is going to increase, namely in the left side of the image, where the main dysfunction lies. Thus, in addition of recording the number of omissions in the upper and lower halves, it will also be important to register the number of omissions in the left and right halves, since it could highlight the severity of the neglect, the bias towards the right ride and possible improvements before and after the intervention (phase 2). It would also be fundamental to analyze the scanning method and compare it to the scanning method of healthy participants and the impact that the size of the icons has on the performance of the HN patients.

A previous study conducted by Warren et al. corroborates these findings [47]. This study analyzed the performance and types of search strategies used by 81 healthy adults in cancellation tasks. The results showed that, similarly to the conclusions of the current study, the participants prioritized a left to right and top to bottom strategy. Also, scores of the participants were extremely high, with error rates and standard deviations similar to the ones obtained in the current study (of the 7 different tests, test 2 presented the highest error with a number of identified object of 38.5 out of 40 and standard deviation of 1.9). A more recent research led by Benjamins et al. investigated the relation between different demographical groups and cancellation task performance, on a total sample of 523 healthy participants [51]. Their conclusions show that age, sex, and level of education do not affect the performance – this is an important conclusion to consider when applying the solution to HN patients. Therefore, several studies regarding cancellation tasks corroborate the results obtained in the current study and validate its applicability.

<u>Clock Test</u>: This test was performed by the participants without any difficulty. They did not display any type of adverse reaction or unforeseen response to the exercise which leads to the conclusion that it is safe to be applied to HN patients.

An experiment led by Berger et al. applied the Clock Test to a sample of 462 participants and revealed that clock drawing tests which require time setting had higher sensitivities and lower misclassification rates (sensitivities of 81 to 93% compared to 58 to 72% obtained by methods that do not require Time Setting; overall misclassification rates of 19 to 25% compared to 30 to 35%) [52]. Thus, when applying this exercise in a clinical practice, the Clock Test should be changed – instead of asking the participant to identify the hour presented on the clock, the participant should be presented with an hour written on the sheet of paper (using a 24 or 12 hour format depending on the nationality or

preference of the participant – for example, 18:35/6:35pm) and then asked to draw a clock with the given hour while maintaining the pointer on each side of the clock to highlight any possible biases arisen from the neglect. This was not done initially because the approach used in this study is the one present in the BIT and allows for a deeper assessment of spatial neglect since telling the hour on the clock requires more spatial capabilities than identifying a written hour. So, although the current use of the Clock Test allows a deeper assessment of spatial independently from motor neglect, the new version should be adopted since it has higher sensitivity and lower overall misclassification rates.

Other studies have also shown that the performance in the Clock Test is highly correlated with the age of the participant [53] [54]. This should be considered in the clinical application of the solution on HN patients, since the errors committed may not only be due to the pathology but also to the decrements of proficiency inherent to old age regarding sight and spatial recognition [55].

When applying this test (with the aforementioned changes) to patients with HN, it is likely that the patient will be able to identify the hour but the drawing of the clock is expected to have large asymmetries prioritizing the right side of the clock, omission of elements in the left side, the average size of the clocks is expected to be smaller than the clocks drawn by healthy participants and their shape is expected to be elliptical instead of circular [56].

<u>Article Reading</u>: An important task to assess the visual capabilities of the participant independently, since it does not require any type of muscular activation. The healthy participants performed the exercise easily, reading the excerpt effortlessly. More importantly, and also as expected, the participants did not show any type of adverse response to the exercise, completing it without any difficulty.

A work done by Lindell et al. assessed the sensitivity and effectiveness of different exercises in evaluating the neglect, including the Article Reading test [57]. It was applied on a sample of 31 healthy participants and 34 patients with a stroke on the right hemisphere. Likewise, the excerpt was divided in 3 columns. The results showed that 100% of the participants without visuo-spatial pathologies performed normally in the task, similarly to the results obtained in the current research (of the healthy participants, 100% showed normal performances – a performance was considered normal if a maximum of 1 word was omitted). Additionally, the Article Reading task was the one which identified the highest number of neglect cases (88%) of all the tasks analyzed.

Therefore, the suitability of this exercise to HN patients is validated since it is one of the few exercises which allows the assessment of spatial neglect without the influence of other aspects of the pathology of the patient (namely motor neglect), does not have any expected negative side effects and, thus, is an efficient task in the evaluation and assessment of HN. When applying this exercise in a clinical setting, the number of omitted words is expected to increase substantially, namely in the left column of the excerpt. The performance is expected to increase after the intervention.

<u>Phase 2</u>: This phase, composed of the AR and auditory tasks, has the goal of improving the HN symptoms when applied to patients with this pathology. The healthy participants in the current study performed all the tasks with ease and expressed satisfaction (behaviorally and verbally).

The results obtained by all the participants can lead to a few conclusions: the cadence of the stimulus is appropriate in all tasks (which was also confirmed verbally by the participants), the color and shape of the AR stimuli is also suitable, the gradients used in the first AR exercise are also adequate, the positions in which the stimuli appears on the AR tasks is appropriate and the auditory stimulus chosen is adequate and perceptible.

However, the claims by some participants regarding the problems with the HMD must be taken into account. These participants asserted that the HMD put too much pressure on the nose which became uncomfortable after some time and needed to hold it with their hands to complete the exercise. Moreover, they also claimed that the HMD defocused the image slightly, which further decreased the immersion and seamlessness of the experience. These reports must be considered prior to the clinical application of this solution in order to present the most effective and comfortable experience to the participants – consider switching the brand of the HMD or, if possible, adapt the ones currently used.

In a clinical application of this solution, the conclusions obtained in the current study are expected to be held true – the cadence of the stimuli and the shape, color and positioning of the AR cues are expected to be adequate. It is expected that this phase will stimulate and induce improvements in the patient's condition. Nonetheless, the performance of HN patients is expected to be worse, with omissions in both exercises, namely omissions of the cues on the left side of the FoV in the AR exercises when these are in the area closer to the periphery of the FoV. Unlike the current study, when applying this solution to HN patients, the training version should be presented to all patients prior to the exercise itself (in the current study, this training version was only presented to the participants who requested it) to provide support, minimize the errors committed and increase performance. Additionally, there were no negative side effects observed on healthy participants. However, it is possible that the patients could experience nausea or dizziness, even though previous work on this field show that the probability of these symptoms happening is extremely low [58]. A participant performing the AR tasks is represented in Figure 15.

Therefore, the results obtained (written and verbally) confirm the pertinence of the solution and, thus, this exercise is also valid for HN patients, with the aforementioned adjustments.



Figure 16: One of the participants performing the AR tasks.

Game Experience Questionnaire: This questionnaire is a central part of this research since it allows the qualitative evaluation of the solution prior to its clinical application. When analyzing the results of the GEQ, it is important to bear in mind the target population group of this solution. Since it is going to be applied, mainly, to people over the age of 65 [48] (since this is the age group more susceptible to stroke), the solution should be pleasant, fluid and seamless (Positive/Negative Affect, Positive/Negative Experience, Sensitive and Imaginative Immersion), intuitive (Competence), of low difficulty (Challenge), it should not cause any discomfort, boredom, tension, nausea or dizziness (Tension/Annoyance, Difficulty Returning to Reality) and should have an appropriate duration so it won't be wearing to the patient (Flow, Tiredness).

In fact, the participants in the current study rated the experience as positive (both in-game and afterwards (Positive Experience/Affect >> Negative Experience/Affect)), easy and accessible (high Competence and low Challenge), comfortable and with an appropriate duration (Tension/Annoyance and Tiredness with scores of 0, low Difficulty Returning to Reality and high Flow). However, it is also important to notice that the Sensitive and Imaginative Immersion component has an intermediate value (2,2 out of 4). This is most likely due to the aforementioned claims of the participants regarding the HMD – the nose pressure and the defocusing done by the glasses reduces the immersion of the experience which justifies the score in this component. The remaining components substantiate the validity and applicability of the solution.

The overall duration of the intervention was around 30 minutes. However, with the adjustments previously proposed (namely to the Cancellation Task), the duration should decrease. Nonetheless, this duration seemed appropriate, since it did not tire the participants, who also expressed satisfaction while performing the different tasks. When applying the solution to HN patients, the total duration is expected to increase since it is expected that the scanning process in the Cancellation Task will be slower, the drawing of the clock and the reading of the article will take longer and the AR and auditory tasks will also take more time since the training version will be presented to every patient.

The intervention induced overall satisfaction in the participants and the previous work done in the field corroborate the applicability of the solution.

5. Conclusion

The goal of the present study was the development of a non-invasive, cross-modal intervention plan aiming to rehabilitate HN patients and the assessment of its applicability through testing on healthy individuals, prior to its clinical application. The outline of this solution was devised after reviewing previous work done in the area of Hemispatial Neglect and associated therapy and rehabilitation strategies. Moreover, it was developed with the support of members from the start-up NEVARO and the solution was validated by Dr. Pedro Alves from the Department of Neurology, *Hospital de Santa Maria*. The work conducted by previous authors, namely by Smith et al. [38] and Hommel et al. [27], substantiated the applicability of virtual and auditory cueing in the amelioration of HN symptoms, laying the foundations for this work, which tried to expand the knowledge in the field using a cross-modal solution that, up to the author's knowledge, hasn't been experimented before.

The solution was designed around the AR and auditory cues, with tasks requiring visuo-spatial capabilities applied before and after this phase to assess changes, oscillations, and possible improvements in the performance of the participants. For a more comprehensive approach, these tasks were chosen in a way which allows the assessment of the spatial and motor neglects independently. Similarly, the strategy employed in the cueing exercises prioritized on stimulating the spatial capabilities (Augmented Reality cues and identifying the ear channel in the auditory cueing exercise) and muscular activation of the participant (raising an upper limb in the second exercise of the auditory cues). At the end of the intervention plan, the participants filled two modules of the Game Experience Questionnaire (Core and Post-Game) – the results obtained from this questionnaire are central to this phase of the research (assessment of the applicability of the solution through testing in healthy individuals) since it quantitively scores qualitative aspects of the solution, elucidating about its robustness and allowing the identification of possible enhancements and/or adjustments to be implemented.

The results from the nine participants validate the applicability of the solution. All tasks were completed without difficulty and the results were near perfect in every task. No adverse or unforeseen reaction was observed in any participant. All these observations regarding the Augmented Reality tasks are corroborated by the results from the GEQ, which further substantiate the strategy's pertinence. The only observations pointed out the long duration of the Cancellation Tasks and the deficiencies of the HMD, which decreased the immersiveness of the experience. Thus, before the clinical application of this intervention plan, the duration of the Cancellation Tasks should be reduced to a number of icons which does not tire or bore the participant. The Bells Test from the Behavioral Inattention Test has 35 total targets and 280 distractors (total of 315 icons) [59]. The applied Cancellation task has 48 targets and 326 distractors in phase 1 and 38 targets and 336 distractors in phase 3 (total of 374 icons). Thus, the size of the Cancellation Task used in this research should emulate the Bells Test in size – the number of targets and distractors must be reduced prior to the clinical application. Regarding the HMD, and as aforementioned, it should either be switched or adjusted in order to solve the identified issues. To choose the best solution, an internet search should be performed to analyze reviews regarding

different HMDs and pick the most proficient one to deliver the most comfortable and immersive experience possible.

After all the adjustments are implemented, the solution will be prepared for the next clinical phase – application in HN patients, since the qualitative and quantitative results obtained from this research corroborate the pertinence and applicability of the strategy.

5.1 Future Work

The work done in this research is, up to the author's knowledge, the first time visual and auditory cues were administered sequentially in an intervention plan aiming to rehabilitate Hemispatial Neglect patients. Since the results obtained point towards the applicability of this novel technique, this work may lay the foundations for further work in the area of HN rehabilitation. Nonetheless, this study constitutes early work and must be validated by testing on HN patients prior its general acceptance.

In future researches based on this study, there are a number of factors and variables that could be explored:

- Larger sample and monitoring over time applying the solution to a larger sample to increase the significance of the results and monitor these results over time to understand the long-term impacts on the patients.
- Record physiological signals perform pertinent medical measurement and recording techniques on the participants while undergoing this intervention plan, namely Electroencephalography (EEG) and Photoplethysmography (PPG), to identify any possible patterns which could provide significant information regarding Hemispatial Neglect.
- Other types of cues using different types of cues, such as tactile or proprioceptive, and compare the results obtained with the current cues could prove useful in identifying the most effective strategy.
- Digitalization of phases 1 and 3 presenting the tasks in these phases via digital support to allow standardization and easier communication between medical facilities.
- Eye Tracking software by using this type of feature, it is possible to measure the eye
 position, point of gaze and the motion of the eye relative to the head. These
 measurements may elucidate regarding the neglect and the coping mechanisms. By
 understanding these mechanisms, it is possible to devise a strategy to tackle the HN at
 a deeper level, focusing on the areas of the FoV more affected by the pathology.

Thus, there are numerous factors that are worth exploring in future researches. The conclusions taken from this future work will aid in formulating the most effective, patient-oriented strategy to rehabilitate Hemispatial Neglect patients in a comfortable and non-invasive way using state-of-the-art technology.

6. References

- [1] A. Riestra and A. Barrett, "Rehabilitation of spatial neglect," *Handbook of Clinical Neurology*, pp. 347-355, 2013.
- [2] K. Li, Malhotra and P. A, "Spatial Neglect," *Practical Neurology*, pp. 15:333-339, April 2015.
- [3] A. Parton, P. Malhotra and M. Husain, "Hemispatial Neglect," *Journal of Neurology, Neurosurgery & Psychiatry*, pp. 75:13-21., May 2004.
- [4] "Left and Right Hemisphere of the Brain," 2019. [Online]. Available: https://humanmemory.net/left-and-right-hemisphere-of-the-brain/. [Accessed April 2020].
- [5] F. S. Leibovitch, S. E. Black, C. B. Caldwell, P. L. Ebert, L. E. Ehrlich and J. P. Szalai, "Brainbehavior correlations in hemispatial neglect using CT and SPECT," *Neurology*, pp. 4:901-908, 1998.
- [6] "Hemineglect," 2008. [Online]. Available: http://www.scholarpedia.org/article/Hemineglect. [Accessed April 2020].
- [7] "Stroke," Mayo Clinic, [Online]. Available: https://www.mayoclinic.org/diseasesconditions/stroke/symptoms-causes/syc-20350113. [Accessed March 2020].
- [8] M. Katan and A. Luft, "Global Burden of Stroke.," *Circulation Research*, pp. 38(2):208-211., April 2018.
- [9] "Global Health Data Exchange," 2020. [Online]. Available: http://ghdx.healthdata.org/gbd-results-tool. [Accessed February 2020].
- [10] V. S. Hedna, A. Bodhit, S. Ansari, A. Falchook, L. Stead, K. Heilman and M. Waters, "Hemispheric differences in ischemic stroke: is left-hemisphere stroke more common?," *Journal of Clinical Neurology*, pp. 9(2): 97-102, 2013.
- [11] M. L. Portegies, M. Selwaness and A. Hofman, "Left-Sided Strokes Are More Often Recognized," *The Roterdam Study*, p. 46:252–254, December 2015.
- [12] P. Plummer, M. E. Morris and J. Dunai, "Assessment of Unilateral Neglect," *Physical Therapy*, p. 732–740, August 2003.
- [13] "Bells Test," Stroke Engine, [Online]. Available: https://www.strokengine.ca/en/assess/bt/. [Accessed March 2020].
- [14] "Hemianopia," Healtline, [Online]. Available: https://www.healthline.com/health/hemianopia#symptoms. [Accessed May 2020].
- [15] D. Ting, A. Pollock, G. Dutton and F. Doubal, "Visual Neglect Following Stroke: Current Concepts and Future Focus," *Survey of Ophthalmology*, pp. 56(2):114-34, March 2011.

- [16] C. Rorden, L. Jelsone, S. Simon-Dack, L. L. Baylis and G. C. Baylis, "Visual Extinction: The effect of temporal and spatial bias," *Neuropsychologia*, pp. 321-329, January 2009.
- [17] T. Silverstone, "Electroencephalogram," *Biological Aspects of Affective Disorders*, pp. 271-303, 1991.
- [18] H. Brinson, "Psychology," *The EEG profile of hemispatial neglect and neurofeedback as an intervention*, 2012.
- [19] R. T. Watson, M. Andriola and K. M. Heilman, "The electroencephalogram in neglect," *Journal of the Neurological Sciences,* pp. 34(3):343-8, December 1977.
- [20] I. H. Robertson, R. Tegnér, K. Tham, A. Lo and I. Nimmo-smith, "Sustained attention training for unilateral neglect: Theoretical and rehabilitation implications," *Journal of Clinical and Experimental Neuropsychology*, pp. 416-430, 1995.
- [21] L. Wiart, A. B. SaintCôme, X. Debelleix and H. P. Pierre, "Unilateral neglect syndrome rehabilitation by trunk rotation and scanning training," *Archives of Physical Medicine and Rehabilitation*, pp. 78(4):424-9, April 1997.
- [22] C. Samuel, A. Louis-Dreyfus, R. Kaschel, E. Makiela, M. Troubat, N. Anselmi, V. Cannizzo and P. Azouvi, "Rehabilitation of very severe unilateral neglect by visuo-spatio-motor cueing: Two single case studies," *Neuropsychological Rehabilitation*, pp. 385-399, 2000.
- [23] I. H. Robertson, K. Hogg and T. M. McMillan, "Rehabilitation of Unilateral Neglect: Improving Function by Contralesional Limb Activation," *Neuropsychological Rehabilitation*, pp. 19-29, 1998.
- [24] B. Olk and M. Harvey, "Effects of visible and invisible cueing on line bisection and Landmark performance in hemispatial neglect," *Neuropsychologia*, pp. 282-290, 2002.
- [25] T. Vleet, M. Van and L. C. Robertson, "Cross-modal Interactions in Time and Space: Auditory Influence on Visual Attention," *Journal of Cognitive Neuroscience*, pp. 18(8):1368-79, August 2006.
- [26] M. E. McCourt, M. Garlinghouse and P. A. Reuter-Lorenz, "Unilateral visual cueing and asymmetric line geometry share a common attentional origin in the modulation of pseudoneglect," *Cortex*, pp. 499-511, 2005.
- [27] M. Hommel, B. Peres and P. Pollak, "Effects of Passive Tactile and Auditory Stimuli on Left Visual Neglect," JAMA Neurology, pp. 47(5):573-576, May 1990.
- [28] G. Vallar, M. Rusconi and E. Bisiach, "Awareness of contralesional information in unilateral neglect: effects of verbal cueing, tracing and vestibular stimulation," *Attention and Performance XV: Conscious and Nonconscious Information Processing*, pp. 377-390, 1994.
- [29] R. Bierig and T. A. L. Myers, "Virtual Reality and Left Hemineglect: A Technology for Assessment and Therapy," *CyberPsychology & Behavior, Vol. 3, No. 3,* pp. 465-468, 2000.

- [30] A. Milner, M. Brechmann and L. Pagliarini, "To halve and to halve not: an analysis of line bisection judgements in normal subjects.," *Neuropsychologia*, pp. 515-526, June 1992.
- [31] M. J. Riddoch and G. W. Humphreys, "The effect of cueing on unilateral neglect," *Neuropsychologia*, pp. 589-599, 1983.
- [32] P. L. Tsai, M. C. Chen, Y. T. Huang, K. C. Lin and K. Lin, "Listening to Classical Music Ameliorates Unilateral Neglect After Stroke," *American Journal of Occupational Therapy, Vol. 67*, pp. 328-335, May 2013.
- [33] "Catherine Bergego Scale," Shirley Ryan Ability Lab, [Online]. Available: https://www.sralab.org/rehabilitation-measures/catherine-bergego-scale-kessler-foundationneglect-assessment-process. [Accessed March 2020].
- [34] "What is Virtual Reality?," Virtual Reality Society, 2017. [Online]. Available: https://www.vrs.org.uk/virtual-reality/what-is-virtual-reality.html. [Accessed March 2020].
- [35] "How Virtual Reality Works," How Stuff Works, 2020. [Online]. Available: https://electronics.howstuffworks.com/gadgets/other-gadgets/virtual-reality.htm. [Accessed March 2020].
- [36] "What is Augmented Reality (AR) and How does it work," Think Mobiles, [Online]. Available: https://thinkmobiles.com/blog/what-is-augmented-reality/. [Accessed March 2020].
- [37] "How Augmented Reality Works," How Stuff Works, 2020. [Online]. Available: https://computer.howstuffworks.com/augmented-reality5.htm. [Accessed March 2020].
- [38] J. Smith, D. Hebert and D. Reid, "Exploring the effects of virtual reality on unilateral neglect caused by stroke: Four Case Studies," *Technology and Disability,* pp. 19(1):29-40, January 2007.
- [39] T. Ogourtsova, W. S. Silva, P. S. Archambault and A. Lamontagne, "Virtual reality treatment and assessments for post-stroke unilateral spatial neglect: A systematic literature review," *Neuropsychological Rehabilitation*, pp. 27(3):1-46, April 2017.
- [40] "Unity Real-Time Development Platform," Unity, [Online]. Available: https://unity.com/. [Accessed 2020].
- [41] "Adobe Premiere," Adobe, [Online]. Available: https://www.adobe.com/pt/products/premiere.html. [Accessed May 2020].
- [42] K. Poels, Y. d. Kort and W. Ijsselsteijn, "D3.3 : Game Experience Questionnaire: development of a self-report measure to assess the psychological impact of digital games," Eindhoven University of Technology, 2007. [Online]. Available: https://research.tue.nl/en/publications/d33-game-experience-questionnaire-development-ofa-self-report-me. [Accessed October 2020].
- [43] "Behavioral Inattention Test," Shirley Rian Ability Lab, [Online]. Available: https://www.sralab.org/rehabilitation-measures/behavioral-inattention-test. [Accessed 2020].

- [44] "Samsung Galaxy A70," [Online]. Available: https://www.samsung.com/pt/smartphones/galaxy-a70-a705/SM-A705FZKUTPH/. [Accessed September 2020].
- [45] "NEVARO," NEVARO-Tech, [Online]. Available: https://nevaro.tech/. [Accessed February 2020].
- [46] "A importância da Leitura," Infoescola, [Online]. Available: https://www.infoescola.com/educacao/a-importancia-da-leitura/. [Accessed April 2020].
- [47] M. Warren, J. M. Moore and L. K. Vogtle, "Search Performance of Healthy Adults on Cancellation Tests," American Journal of Occupational Therapy, Vol. 62, pp. 588-594, 2008.
- [48] "The Internet Stroke Center," [Online]. Available: http://www.strokecenter.org/patients/aboutstroke/stroke-statistics/. [Accessed October 2020].
- [49] J. v. Deusen, "Normative Data for Ninety-Three Elderly Persons on the Schenkenberg Line Bisection Test," *Physical & Occupational Therapy In Geriatrics, Vol. 3,* pp. 49-54, 1985.
- [50] L. Gamberini, B. Seraglia and K. Priftis, "Processing of peripersonal and extrapersonal space using tools: Evidence from visual line bisection in real and virtual environments," *Neuropsychologia*, pp. 1298-1304, 2008.
- [51] J. Benjamins, E. Dalmaijer, A. T. Brink, T. Nijboer and S. V. d. Stigchel, "Multi-target visual search organisation across the lifespan: cancellation task performance in a large and demographically stratified sample of healthy adults," *Aging, Neuropsychology, and Cognition, Vol. 26,* pp. 731-748, 2018.
- [52] G. Berger, L. Frolich, B. Weber and J. Pantel, "Diagnostic Accuracy of the Clock Drawing Test: The Relevance of ``Time Setting'' in Screening for Dementia," *Journal of Geriatric Psychiatry and Neurology*, pp. 250-260, 2008.
- [53] V. Turcotte, M.-E. Gagnon, S. Joubert, I. Rouleau, J.-F. Gagnon, F. Escudier, L. Koski, O. Potvin, J. Macoir and C. Hudon, "Normative data for the Clock Drawing Test for French-Quebec mid- and older aged healthy adults," *The Clinical Neuropsychologist*, pp. 91-101, May 2018.
- [54] A. F. Mazancova, T. Nikolai, H. Stepankova, M. Kopecek and O. Bezdicek, "The Reliability of Clock Drawing Test Scoring Systems Modeled on the Normative Data in Healthy Aging and Nonamnestic Mild Cognitive Impairment," *Sage Journals*, pp. 250-260, December 2016.
- [55] D. Quillen, "Common Causes of Vision Loss in Elderly Patients," *American Family Physician*, pp. 60(1):99-108, 1999.
- [56] P. Chen and K. M. Goedert, "Clock Drawing in Spatial Neglect: A Comprehensive Analysis of Clock Perimeter, Placement, and Accuracy," *Journal of Neuropsychology*, pp. 270-289, March 2012.
- [57] A. B. Lindell, M. J. Jalas, O. Tenovuo, T. Brunila, M. J. M. Voeten and H. Hämäläinen, "Clinical Assessment of Hemispatial Neglect: Evaluation of Different Measures and Dimensions," *The Clinical Neuropsychologist*, pp. 479-497, April 2007.

- [58] C. Moro, Z. Stromberga, A. Raikos and A. Stirling, "The Effectiveness of Virtual and Augmented Reality in Health," *Anatomical Sciences Education*, pp. 549-559, April 2017.
- [59] L. Zeltzer and A. Menon, "Bells Test," Stroke Engine, November 2011. [Online]. Available: https://strokengine.ca/en/assessments/bells-test/. [Accessed November 2020].
- [60] Microsoft, "Microsoft Power BI," [Online]. Available: https://powerbi.microsoft.com/pt-pt/. [Accessed October 2020].

7. Appendices

7.1 Appendix A. Exercise Sheets, Phase 1

Fase 1						
	Por favor,	identifique o pon	to médio de o	cada uma das	linhas.	
			-			

Figure 17: Line Bisection exercise sheet for phase 1.

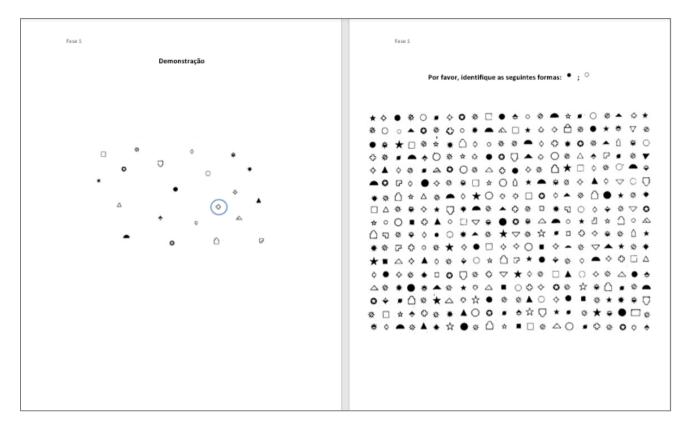


Figure 18: Cancelation Task exercise sheet for phase 1.

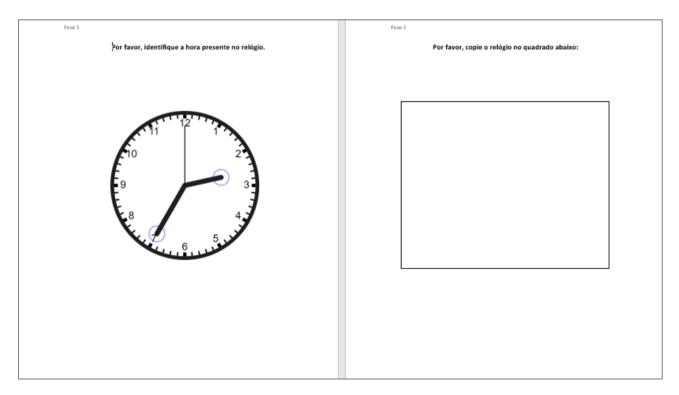


Figure 19: Clock Test exercise sheet for phase 1.

Fase 1

Por favor, leia o seguinte excerto de texto em voz alta.

Muitos são os benefícios que a leitura proporciona: desenvolvimento da imaginação, da criatividade, da comunicação, bem como o aumento do vocabulário, conhecimentos gerais e do sentido crítico. Além desses benefícios, com a leitura exercitamos o nosso cérebro, o que facilita a interpretação de textos e leva à maior a competência na escrita. Ao ler, o indivíduo adquire maior repertório, ampliando e expandindo os seus horizontes cognitivos. Para além disso, estudos apontam que o ato de ler é muito útil na medida em que reduz o stress ao mesmo tempo que estimula reflexões e introspeção. Por esse motivo, a leitura deve ser incentivada desde a educação primária. Incentivar os filhos pequenos em casa e criar hábitos são métodos importantes para que as crianças desenvolvam o gosto pela leitura.

Figure 20: Article Reading exercise sheet for phase 1.

7.2 Appendix B. Exercise Sheets, Phase 3

Fase 3			
P	or favor, identifique o ponto	médio de cada uma das linl	nas.

Figure 21: Line Bisection exercise sheet for phase 3.

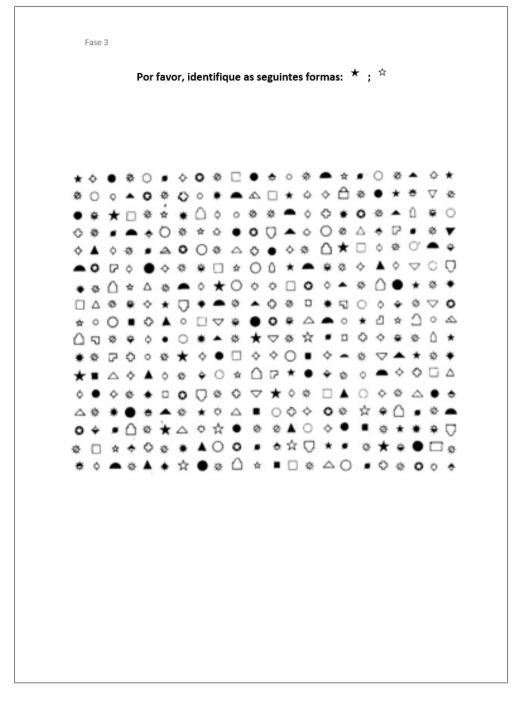


Figure 22: Cancelation Task exercise sheet for phase 3.

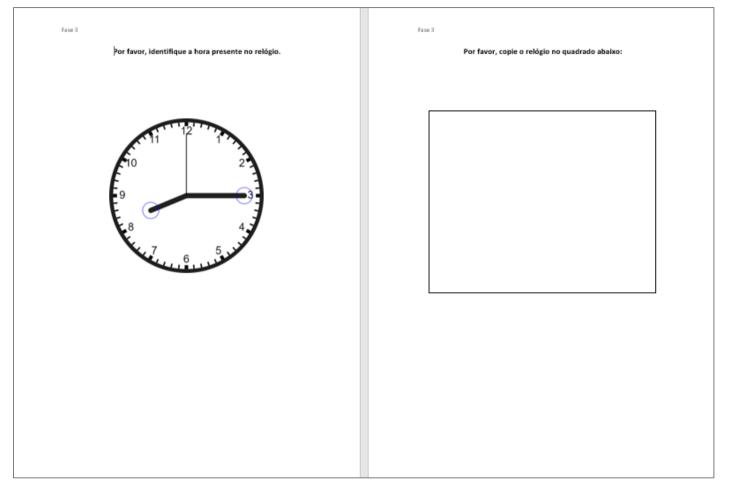


Figure 23: Clock Test exercise sheet for phase 3.

Por favor, leia o seguinte excerto de texto em voz alta.

A leitura é a maneira mais antiga – e mais eficiente, até hoje, de adquirir conhecimento. E é preciso esquecer a ideia de que ler é um hábito chato e monótono. Ao contrário do que muitas pessoas acreditam, ler revistas, livros de romance, entre outras leituras de entretenimento, é tão eficaz quanto ler um livro técnico. A diferença é que ler sobre algo técnico oferece conhecimento sobre determinado assunto, enquanto ler sobre variedades estimula o raciocínio e melhora o vocabulário. A leitura melhora a aprendizagem dos estudantes, pois estimula o bom funcionamento da memória, melhora a capacidade interpretativa, além de proporcionar ao leitor um conhecimento amplo e diversificado sobre vários temas. Quem lê conversa sobre qualquer coisa, e consegue formar opiniões bem fundamentadas.

Figure 24: Article Reading exercise sheet for phase 3.

7.3 Appendix C. GEQ and Results Sheet

Nome:

17 I felt successful 18 I felt imaginative

20 I enjoyed it

23 I felt pressured24 I felt irritable25 I lost track of time

29 I felt frustrated

32 I felt time pressure

19 I felt that I could explore things

22 I felt annoyed (aborrecido/a)

26 I felt challenged (desafiado/a) 27 I found it impressive

30 It felt like a rich experience

33 I had to put a lot of effort into it

28 I was deeply concentrated in the game

31 I lost connection with the outside world

21 I was fast at reaching the game's targets

Game Experience Questionnaire – Core Module

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

scale:			2	2	
not at all 0 < >	slightly 1 < >	moderately 2 < >	fairly 3 < >	extremely 4 < >	
1 I felt content	(satisfeito/a))			
2 I felt skilful (ř	nabilidoso/a)				
3 I was interes	ted in the ga	ime's story			
4 I thought it w	as fun				
5 I was fully oc	cupied with	the game			
6 I felt happy					
7 It gave me a	bad mood				
8 I thought abo	out other thin	igs			
9 I found it tire	some (cansa	ativo)			
10 I felt compe	tent				
11 I thought it	was hard				
12 It was aesth	netically (est	eticamente) plea	sing		
13 I forgot eve	rything arou	nd me			
14 I felt good					
15 I was good	at it				
16 I felt bored					
	not at all 0 <>> 1 I felt content 2 I felt skilful (f 3 I was interes 4 I thought it w 5 I was fully ou 6 I felt happy 7 It gave me a 8 I thought abo 9 I found it tree 10 I felt competing 11 I thought it 12 It was aest 13 I forgot eve 14 I felt good 15 I was good	not at all slightly 0 1 <> <> <> 1 I felt content (satisfeito/a) 2 I felt skilful (habilidoso/a) 3 I was interested in the ga 4 I thought it was fun 5 I was fully occupied with 6 I felt happy 7 It gave me a bad mood 8 I thought about other thin 9 I found it tiresome (cansa 10 I felt competent 11 I thought it was hard 12 It was aesthetically (est 13 I forgot everything around 14 I felt good 15 I was good at it	not at all slightly moderately 0 1 2 <> <> <> <> <> <> <> <> <> <> <> <> <> <	not at all slightly moderately fairly 0 1 2 3 <> <> <> <> <> <> <> <> <> <> <> <> <> <	not at all slightly moderately fairly extremely 0 1 2 3 4 > > > > > > > > > > > > > > > > > > >

Post-Game

1 I felt revived	
2 I felt bad	
3 I found it hard to get back to reality	
4 I felt guilty	
5 It felt like a victory	
6 I found it a waste of time	
7 I felt energized	
8 I felt satisfied	
9 I felt disoriented	
10 I felt exhausted	
11 I felt that I could have done more useful thing	s
40.1 fell a superful	

- 12 I felt powerful 13 I felt weary
- 15 Field wears
- 14 I felt regret
- 15 I felt ashamed
- 16 I felt proud
- 17 I had a sense that I had returned from a journey

Figure 25: Game Experience Questionnaire.

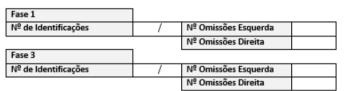
Nome (Codificado): Data:

Line Bisection

Fase 1: distância ao ponto médio	Esquerda:	Centro:	Direita:
Fase 3: distância ao ponto médio	Esquerda:	Centro:	Direita:

Aspetos Qualitativos:

Task Cancellation



Aspetos Qualitativos:

Clock Test



Aspetos Qualitativos:

Muitos são os beneficios que a leitura proporciona: desenvolvimento da imaginação, da criatividade, da comunicação, bem como o aumento do vocabulário. conhecimentos gerais e do sentido crítico. Além desses beneficios, com a leitura exercitamos o nosso cérebro, o que

Aspetos Qualitativos:

facilita a interpretação de

Fase 1 - Riscar omissões

textos e leva à maior a competência na escrita. Ao ler, o indivíduo adquire maior repertório, ampliando e expandindo os seus horizontes cognitivos. Para além disso, estudos apontam que o ato de ler é muito útil na medida em que reduz o stress ao mesmo

tempo que estimula reflexões e introspeção. Por esse motivo, a leitura deve ser incentivada desde a educação primária. Incentivar os filhos pequenos em casa e criar hábitos são métodos importantes para que as crianças desenvolvam o gosto pela leitura.

Fase 3 – Riscar omissões

A leitura é a maneira mais A leitura é a maneira mais antiga – e mais eficiente, até hoje, de adquirir conhecimento. E é preciso desconstruir a ideia de que ler é um hábito chato e monótono. Ao contrário do que muitas pessoas acreditam, ler revistas, livros de romance, entre outras leituras de entretenimento, é tão

Aspetos Qualitativos:

eficaz quanto ler um livro técnico. A diferença é que ler sobre algo técnico oferece conhecimento sobre determinado assunto, enquanto ler sobre variedades estimula o raciocínio e melhora o vocabulário. A leitura melhora a aprendizagem dos estudantes, pois estimula o bom

funcionamento da memória, melhora a capacidade interpretativa, além de proporcionar ao leitor um conhecimento amplo e diversificado sobre diversos temas. Quem lê conversa sobre qualquer coisa, e consegue formar opiniões bem fundamentadas.

Figure 26: First and Second pages of the Results Sheets.

Fase 2 – Guia dos estímulos

Time Intervals		Sphere1 (Right)	(🖌 /X)	Time Intervals			Cylinder 🖌 🖊	Estímulo	(🗸 /X)	Estímulo	(✔/X)
Initializing(15s)	x	x		Initializing (15s) 2s	x	×	x	Bilateral		Starts at: 3s	
2		x		15	x						
2		-		25				Esquerda		After 3s	
1	x			1s 2s		×		Direita		After 2s	
2	x	x		1s			x	Esquerda		After 2s	
2				2s 1s			×	Esquerda		After 1s	
2	x			25			-				
1	x	x		1s	x			Bilateral		After 3s	
2				2s 1s			×	Esquerda		After 2s	
2	x			25			<u> </u>	Direita		After 3s	
1		x		1s 2s		×		Bilateral		After 1s	
1	x			15			x	Esquerda	_	After 2s	
2				2s 1s							
1	x	x		25	x			Esquerda		After 1s	
1		x		1s		×		Direita		After 3s	
2 1, pas 2				2s 1s	×			Bilateral		After 2s	
1, pas 2 2	x	x		25				Esquerda		After 2s	
1	x			1s 2s	x			Esquerda	_	After 3s	
1	x			1s			x				_
2				25				Direita		After 1s	
1		x		1s 2s		×		Bilateral		After 2s	
2	×	×		25 15		×		Direita		After 1s	
2	_			2s 1s				Esquerda		After 3s	
1	x			22	x			Loquerua			

Scoring

Core Module

Competence: Items 2, 10, 15, 17, and 21. Sensory and Imaginative Immersion: Items 3, 12, 18, 19, 27, and 30. Flow: Items 5, 13, 25, 28, and 31. Tension/Annoyance: Items 22, 24, and 29. Challenge: Items 11, 23, 26, 32, and 33. Negative affect: Items 7, 8, 9, and 16. Positive affect: Items 1, 4, 6, 14, and 20.

Competence -Sensory and Imaginative Immersion -Flow -Tension/Annoyance -Challenge -Negative affect -Positive affect -

Post-Game

Positive Experience: Items 1, 5, 7, 8, 12, 16 Negative experience: Items 2, 4, 6, 11, 14, 15. Tiredness: Items 10, 13. Returning to Reality: Items 3, 9, and 17.

Positive Experience -Negative experience -Tiredness -Returning to Reality -

Figure 27: Part of the Third and Fourth pages of the Results Sheet.

7.4 Appendix D. Informed Consent and Informative Sheet







CONSENTIMENTO INFORMADO, ESCLARECIDO E LIVRE para Investigação Clínica

Parte Informativa

1. Titulo do projecto:

Realidade aumentada aplicada ao diagnóstico e avaliação da Síndrome de Negligência Hemiespacial em doentes com AVC

2. Descrição do projecto, sua natureza e objetivo:

O objetivo do projeto é avaliar a aplicabilidade de testes de Realidade Aumentada na avaliação da Negligência Hemiespacial em doentes com Acidente Vascular Cerebral. A avaliação consistirá na aplicação de:

 a) Testes tipo "papel e caneta", já usados habitualmente em contexto clínico na avaliação da negligência hemiespacial.

b) Testes de Realidade Aumentada com estímulos visuais e tarefas com estímulos auditivos: serão colocados no paciente os óculos de Realidade Aumentada, incorporados com o telemóvel contendo as tarefas a testar. O paciente realizará então as tarefas que lhe são propostas (identificar estímulos visuais em diferentes partes do campo de visão). Na segunda tarefa, irão ser colocados auscultadores no paciente de modo a realizar as tarefas auditivas. O paciente deverá identificar os estímulos auditivos que lhe são apresentados.

Todo o material será desinfetado antes e depois da realização de cada tarefa.

1

Beneficios:

O estudo tem como principal objetivo estudar a aplicabilidade e tolerabilidade da tarefa. Só em eventuais estudos futuros se testará a sua eficácia como estratégia de reabilitação. Não se prevê assim um benefício direto para o participante deste estudo. Espera-se, contudo, no futuro que contribua para a melhoria das estratégias de reabilitação de doentes com negligência hemiespacial.

4. Riscos graves e riscos frequentes:

Tonturas, vertigens ou náuseas provenientes da utilização de Realidade Aumentada, apesar de estudos prévios na área provarem que a probabilidade de ocorrência destes efeitos adversos seja reduzida.

Figure 28: First page of the Informed Consent.







2

Parte declarativa do profissional

Confirmo que expliquei à pessoa abaixo indicada, de forma adequada e inteligível, os procedimentos necessários ao ato referido neste documento. Respondi a todas as questões que me foram colocadas e assegurei-me de que houve um período de reflexão suficiente para a tomada da decisão. Expliquei que pode pedir para interromper ou mesmo desistir, caso sinta necessidade ou vontade de o fazer, sem que daí advenha qualquer prejuízo no contexto da sua assistência clinica. Informei que para conforto e respeito da sua privacidade, os dados que me irá fornecer, permanecerão confidenciais e anónimos.

Nome legível do profissional de saúde: [

Unidade de Saúde

Contato institucional do profissional de saúde

À Pessoa/representante

Por favor, leia com atenção todo o conteúdo deste documento. Não hesite em solicitar mais informações se não estiver completamente esclarecido/a. Verifique se todas as informações estão corretas. Se tudo estiver conforme, então assine este documento.

Parte declarativa da pessoa que consente

Declaro ter compreendido os objetivos de quanto me foi proposto e explicado pelo profissional de saúde que assina este documento, ter-me sido dada oportunidade de fazer todas as perguntas sobre o assunto e para todas elas ter obtido resposta esclarecedora, ter-me sido garantido que não haverá prejuízo para os meus direitos assistenciais se eu recusar esta solicitação, e ter-me sido dado tempo suficiente para refietir sobre esta proposta. Autorizo/Não autorizo (riscar o que não interessa) o ato indicado.

Nome:	1
/	

Figure 29: Second page of the Informed Consent







SE NÃO FOR O PRÓPRIO A ASSINAR POR IDADE OU INCAPACIDADE (se o menor tiver discernimento deve também assinar em cima)

Nоме:

Doc. Identificação N.º Data ou Validade /......

GRAU DE PARENTE 8CO OU TIPO DE REPRE 8ENTAÇÃO:

Assinatura

Nota: Este documento é feito em duas vias – uma para o processo/estudo e outra para ficar na posse de quem consente.

Adaptado da Norma nº 015/2013 de 03/10/2013 atualizada a 04/11/2015

Figure 30: Third page of the Informed Consent.







Folheto Informativo

PROJECTO: Realidade aumentada aplicada ao diagnóstico e avaliação da Síndrome de Negligência Hemiespacial em doentes com AVC

INVESTIGADOR RESPONSÁVEL: Ricardo Brito

Vimos desta forma convidá-la/o a participar no nosso estudo de investigação focado em desenvolver uma ferramenta capaz melhorar sintomas de Negligência Hemiespacial, utilizando tecnologias inovadoras como Realidade Aumentada.

Antes de decidir, gostaríamos de lhe apresentar os detalhes desta investigação, a sua razão de ser, a sua utilidade potencial e as implicações da sua participação. Um membro da equipa da investigação irá acompanhá-lo na leitura deste folheto e responderá a quaisquer perguntas que queira fazer.

1 - Em que consiste o estudo "NEHAB - Ferramenta para a reabilitação de pacientes com Negligência Hemiespacial"?

Este estudo tem como objetivo avaliar a aplicabilidade de um plano de intervenção modelado para a avaliação de Negligência Hemiespacial, utilizando Realidade Aumenta e estímulos auditivos.

Esta experiência consistirá na aplicação de:

Testes de papel e caneta, já habitualmente usados em contexto clínico na avaliação da negligência hemiespacial. A duração desta fase estará entre os 10 e 15 minutos.

Tarefas de Realidade Aumentada com estímulos visuais e tarefas com estímulos auditivos: serão colocados no paciente os óculos de Realidade Aumentada, incorporados com o telemóvel contendo as tarefas a testar. O paciente realizará então as tarefas que lhe são propostas identificar estímulos visuais em diferentes partes do campo de visão. Na segunda tarefa, irão ser colocados auscultadores no paciente de modo a realizar as tarefas auditivas. O paciente deverá identificar os estímulos auditivos que lhe são apresentados. Cada um dos testes na segunda fase tem uma duração de aproximadamente 2 a 3 minutos.

Todo o material utilizado será desinfetado antes e depois da realização de cada tarefa.

Os dados recolhidos serão utilizados para estudos académicos, no contexto da tese de mestrado do investigador responsável Ricardo Brito, e também para, caso se identifique aplicabilidade da estratégia, no futuro, desenvolver uma ferramenta de reabilitação para Negligência Hemiespaçial no contexto da start-up Nevaro, spin-off da Faculdade de Ciências da Universidade de Lisboa. Os dados pessoais serão codificados pelo investigador Ricardo Brito, não estando acessíveis a mais nenhum membro da equipa de investigação.

2 - Tenho de participar neste estudo?

A participação no estudo é totalmente voluntária. Vamos descrever o estudo e apresentar o conteúdo deste folheto informativo, incluindo os detalhes da sua participação. Se concordar em participar, ser-lhe-ão apresentadas cópias deste documento e do Formulário de Consentimento informado.

Figure 31: First page of the Informative Sheet.







3 - E se eu desejar desistir do estudo?

É livre de desistir, en qualquer altura, sem ter de fornecer quaisquer razões ou explicações.

4 - O que terei de fazer no âmbito do estudo?

No âmbito do estudo, irá realizar uma sequência de testes de papel e caneta, seguidos de tarefas realizadas com recurso a Realidade Aumentada e estímulos auditivos, todos desenvolvidos de modo a garantir a segurança e conforto do participante.

5 - Quais as desvantagens e riscos de participar?

Possíveis tonturas, vertigens ou náuseas causadas pela utilização de Realidade Aumentada, apesar de estudos prévios na área provarem que a probabilidade destas desvantagens é reduzida. A expectativa da equipa de investigação é de que as sessões em que participar sejam uma experiência agradável.

6 - Quais os possíveis benefícios de participar?

O seu envolvimento irá ajudar a desenvolver/melhorar uma ferramenta de combate à Negligência Hemiespacial, que poderá ter impactos extremamente positivos em futuros casos desta doença. Irá ajudar na melhoria do diagnóstico e recuperação da condição sem qualquer desconforto e através de técnicas não invasivas, algo que ainda não está disponível em ambiente hospitalar.

7 - O que acontece quando o estudo terminar?

Os dados recolhidos irão ser estudados e analisados pelo investigador de modo a desenvolver todos os ajustes sugeridos pelos mesmos para obter a solução mais eficaz. Se desejar saber detalhes sobre os resultados e implicações do estudo, ser-lhe-á enviada uma cópia do relatório do estudo.

8 - E se ocorrer algum problema?

Se tiver alguma preocupação sobre qualquer aspeto deste estudo, deve falar com o investigador Ricardo Brito, que fará o seu melhor para o/a elucidar e responder às suas dúvidas, pessoalmente durante a fase presencial do estudo ou por e-mail, <u>ricardo.de.brito@tecnico.ulisboa.pt</u>.

9 - A minha informação será mantida confidencial?

Sim. Seguiremos todas as práticas éticas e legais e toda a informação sobre si será tratada de forma absolutamente confidencial. Para garantir a anonimidade, os registos pessoais estarão apenas disponíveis na sua integralidade, para o investigador responsável, e os membros da

Figure 32: Second page of the Informative Sheet.







equipa de investigação apenas terão acesso aos dados que necessitarem de conhecer. Se os seus dados forem usados para publicações ou apresentações, serão totalmente anonimizados, sem qualquer referência, direta ou indireta, à sua identidade. Se forem tiradas fotografias, e for nossa intenção usá-las em alguma apresentação, ser-lhe-á pedida autorização prévia. Se estiver disponível para que usemos fotografias ou vídeos para esse propósito, pedir-lhe-emos primeiro que assine autorizações específicas com esse objetivo.

10 - Quem posso contactar relacionado com este estudo?

Ricardo Brito	Prof. Hugo Ferreira
Instituto Superior Técnico da	Faculdade de Ciências da
Universidade de Lisboa	Universidade de Lisboa
<u>ricardo.de.brito@tecnico.ulisboa.pt</u>	<u>hugoferreira@campus.ul.p</u> t

Sinta-se à vontade para os contactar em qualquer matéria relacionada com este estudo.

Muito Obrigado.

Obrigado por nos ter dedicado este seu tempo e por considerar participar neste estudo.

O Investigador Responsável

Figure 33: Third page of the Informative Sheet.