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A Study of Virtual Reality-Mediated Affective State and Cognitive Decline in Alzheimer's Disease

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How Virtual Reality can help Alzheimer’s Disease: A Study of Affective State and Cognitive Decline

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Résumé

La démence de type d'Alzheimer est la plus commune des démences. Elle entraîne un déclin dans les capacités cognitives et fonctionnelles, se traduisant dans des difficultés au niveau de la prise de décision, de l'accomplissement de tâches quotidiennes, de la communication ainsi qu'au niveau de la mémoire et de l'attention. On remarque également une diminution de l'état émotionnel et une apathie chez ces patients. Ce mémoire explore une nouvelle approche pour atténuer les effets psychologiques et cognitifs de la maladie.

Les recherches effectuées dans ce mémoire explorent les impacts cognitifs et les effets sur le bien-être d'une intervention utilisant la réalité virtuelle sur les personnes souffrant de déclin cognitif subjectif. Deux environnements virtuels ont été testés : le premier étant un environnement dans lequel le participant voyage en train à travers différents climats, et le second étant un environnement de musicothérapie qui s'adapte en fonction de la réponse émotionnelle du participant. Pour mesurer les impacts sur l'état affectif, des lectures électroencéphalographiques ont été prises et analysées afin de déduire l'émotion ressentie par le participant avant, pendant et après l'expérience. Les résultats montrent une amélioration générale de l'état émotionnel pour les deux environnements. Quant à la mesure des effets sur les fonctions cognitives, des tâches d'attention et de mémoire ont été effectuées par les participants avant et après l'immersion. Les résultats montrent une légère amélioration des capacités d'attention et une meilleure amélioration de la mémoire. Nous approprions cet écart dans l'expérience de musicothérapie à l'activation musicale d'un réseau de structures cérébrales impliquées dans les expériences agréables : le circuit de récompense. Nous proposons que la musique facilite la rétention de la mémoire chez les personnes souffrant de démence.

En effet, les résultats de l'amélioration des fonctions cognitives pour les deux expériences précédentes dépendent fortement de la précision de l'outil de mesure cognitive utilisé pour évaluer les performances d'attention et de mémoire avant et après l'intervention. Pour assurer cette précision, ce mémoire présente un outil de mesure des performances cognitives basé sur des tâches cognitives qui ont montré à plusieurs reprises leur fiabilité. Cet outil d'adresse aux personnes atteintes de la maladie d'Alzheimer pré-clinique et diagnostiquée.

Mots-clés: Maladie d'Alzheimer, Réalité Virtuelle, Mémoire, Attention, Cognition, Émotions, Thérapie par musique, Thérapie par voyage, Enregistrements EEG.

Abstract

Alzheimer's disease is an irreversible disease which causes progressive memory loss and cognitive decline, eventually leading to severe inability to perform basic day-to-day tasks. The urgency to find an effective cure to the disease is crucial, as the medical and economical spin-offs could be disastrous. The present thesis explores a novel approach to help attenuate the psychological and cognitive effects of the disease.

The research carried out for this thesis explored cognitive effects and impacts on overall well-being of a virtual reality intervention on people suffering from subjective cognitive decline. Two virtual environments were tested: the first being an environment in which the participant travels through different climates by train, and the second being a music therapy environment modified as a function of emotional response. To measure the effects on affective state, electroencephalography readings were taken and analyzed to infer the emotion felt by the participant before, during the experiment. Results show a general improvement in emotional state. To measure the effects of the environments on cognitive functions, attention and memory tasks were carried out by the participants before and after the immersion. Results show a small improvement in attention skills and a more substantial improvement in memory skills. We appropriate this discrepancy in the music therapy experiment to the musical activation of a network of brain structures involved in rewarding and pleasurable experiences. We propose that music could facilitate memory retention in people sufferance for dementia.

Importantly, the results of the previous experiments rely heavily on the accuracy of the cognitive measurement tool used to evaluate attention and memory performances before and after the intervention. To provide this accuracy, this thesis presents a cognitive performance measurement tool based on cognitive tasks which have repeatedly shown to output reliable results. This tool is created to serve for people with pre-clinical Alzheimer's disease and diagnosed Alzheimer's disease. Additionally, this tool is designed in such a way as to minimize the effects of repetition as well as varying levels of education and language.

This thesis presents a novel and promising research in the realms of computer sciences and health care

Keywords: Alzheimer's Disease, Virtual Reality, Memory, Attention, Cognition, Emotion, Music Therapy, Travel Therapy, EEG Recordings.

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List of acronyms and abbreviations

AD	Alzheimer’s disease
AI	Artificial intelligence
BRS	Brain reward system
EEG	Electroencephalography
IA	Intelligent agent
IUGM	Institut universitaire de gériatrie de Montréal
MCI	Mild cognitive impairment
MT	Music therapy
SCD	Subjective cognitive decline
VE	Virtual environment
VR	Virtual reality

This thesis is wholeheartedly dedicated to my grandfather, Maurice Byrns,

who battled against Alzheimer's disease.

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Chapter 1. Introduction

1.1. General Context and Motivations

Alzheimer's disease (AD) is a neurodegenerative disease which causes unmistakable memory decline and cognitive impairments. While its causes are not fully understood, it is generally accepted that genetics, environment, and lifestyle play a role in its onset [1], [2]. Age, though, is arguably the biggest risk factor for AD [3].

With our ageing population, new cases of the disease are increasing at an important rate. Without effective treatment, repercussions on our health systems, social support systems and our economy could be disastrous [4], [5]. Our current situation calls for important actions, and perhaps uniting different areas of research to find multidisciplinary solutions is what will increase our chances of finding effective treatments.

Decades of research have shone light on the intricacies of the disease. On a physiological level, lesions in key areas of the brain spread along with the progression of the disease, causing cellular death and synaptic dysfunctions [6]. These irreversible damages in turn cause important memory, attention, and other cognitive impairments [7]. The severity of these symptoms increases as individuals enter the later stages of the disease. Eventually, patients have trouble recognizing loved ones, become bedridden and unable to perform everyday tasks [8].

On an emotional level, AD causes alterations in emotional processing [9], recognition [10], and overall experience. The most common neuropsychiatric symptom of the disease is apathy: a state of reduced motivation accompanied by reducing initiative, interest and emotional responsiveness [11]. Other common symptoms are depression, aggression, anxiety and sleep disorder [12]. Unsurprisingly, wellbeing and quality of life of both patients and caregivers are greatly influenced by the emotional changes brought on by the disease. Interestingly, in addition to diminished well-being, some studies have shown that negative emotions decrease cognitive performance in multiple domains, such as memory and attention skills [13], suggesting that cognitive decline can be amplified by other symptoms of the disease.

While there are currently no treatments, medical research has developed pharmacological treatments to help reduce de severity of some symptoms of the disease, such as depression and anxiety, consequently increasing patient well-being. While these treatments do help, they do not stop or prevent the progression of the disease, and they sometimes generate unwanted side effects or are unusable due to medicinal interactions concerning the patients pre-existing health conditions. Thankfully, effective treatments for symptoms such as anxiety and depression are not limited to pharmacological treatments. Indeed, multiple non-invasive treatments, such as music and art therapy, have shown positive results and can be used in a larger population due to their absence of side effects or incompatibility with other medication. The problem with these treatments, though was that we thought they couldn't provide any cognitive rehabilitation. We were wrong.

Recent research has put forth brain plasticity theories shining light on the brain's ability to reconstruct when interacting with enriched environments. More specifically, the nervous system is capable of reconstructing cellular synapses – the contact between neurons, which enables the flow of information through the brain – which could in turn promote cognitive rehabilitation [14], [15].

The benefits of some non-invasive therapies, which include improved affective state and potential cognitive rehabilitation, combined with the absence of medically induced side effects represents a perfect candidate for the investigation of new treatments for AD. In this regard, virtual reality is quickly gaining interest due to the numerous advantages it offers. As an easily accessible, inexpensive, and easy to use technology, both users and researchers benefit from the experience. On the one hand, users generally enjoy the experience, which increases the likelihood of them repeating the experience and benefiting from the outcomes. On the other hand, researchers obtain complete control over the user's environment, which enables them to carefully tailor the experiment as they envision it. This helps experiments run more smoothly and have less uncontrollable variables which could alter results.

Much research has already shown the potential and efficacy of VR in a wide range of psychiatric disorders [16]. For example, VR treatments can be used as exposure therapy for people experiencing phobias. In such situations, people can confront their phobia – such as spiders or heights – through the VR headset, eliminating any potential danger. Similarly, VR exposure therapy has been successfully used to help military personnel suffering from PTSD [17]. Other conditions, such as hemiparetic cerebral palsy [18], psychosis [19] and other psychological and physical disorders [20] have benefited from VR therapies.

An important feature we believe lacks in most of the studies using VR for therapeutic means is the virtual environment's (VE) ability to evolve and adapt itself as a function of the participant. More specifically, we believe that monitoring emotions and adapting the virtual experience as a function of them is of great importance. Since the reduction of negative emotions has in some cases shown to promote better cognitive performances in addition to increase wellbeing, there is some potential as to the benefits of this type on intervention on cognitive functions.

In this research, we design, develop, and test two virtual environments on individuals suffering from subjective cognitive decline (SCD). We chose to carry out this investigation on individuals suffering from SCD because this population is at greater risk of developing the disease, making these individuals more likely to be in the pre-clinical phases of AD [21]. It has been repeatedly proposed that therapeutic intervention should target individuals suffering from pre-clinical AD [22], since intervening at the very early stages of the disease may potentially delay, stagnate or ideally reduce some symptoms and impairments brought on by the disease. The works of this research were made possible with the collaboration of staff from the Institut Universitaire de Gériatrie de Montréal (IUGM). Indeed, after obtaining the ethics committee's approval, staff from the IUGM recruited and booked appointments with interested and eligible individuals. On experimentation days, our lab's team, namely Hamdi Ben Abdesslem and Marwa Boukadida, brought all of the experimental equipment and met participants at the IUGM. During the session, our team made sure to carefully follow the experimental protocol, including signing consent forms, installing the equipment and carrying out the experiment.

The first environment replicates a train traveling through different scenarios. This environment requires no active participation from the participant and is not adapted to the user in any way. For the second environment, we designed in a VE the already-existing intervention music therapy (MT), as it has already proven to be effective for people suffering from AD [23]–[25]. In an attempt to improve and optimize the utilization of VR, this environment integrates an intelligent agent capable of modifying the environment appropriately as a function of emotional states.

To accurately monitor the cognitive effects of the environments, it is important to have a tool capable of accurately measuring cognitive skill progression through time while limiting the effects of practice. Indeed, some cognitive tasks can be more easily and accurately completed if the same task has been repeatedly done. Consequently, the repetition of these tasks as a measurement of cognitive function does not accurately represent the true cognitive state of the participant, as there is a bias due to the practice effect. To this end, this research project explores the design and creation of such a tool capable of measuring cognitive performance improvements through time.

This research is at the intersection of computer science, neuroscience, psychology and artificial intelligence (AI). With contributions from medical experts and computer science experts alike, this thesis proposes two immersive virtual environments (VE) and explores the emotional and cognitive impacts of these VEs on individuals experiencing subjective cognitive decline (SCD). Furthermore, we explore a tool capable of reliably measuring cognitive state and its progression through time.

1.2. Research Goals

In the context of this research project, my objectives are the following:

1. Is it possible to reduce negative emotions through virtual environments?
2. Do the virtual environments improve cognitive functions?

To reach our objectives, we design two virtual environments and test them on participants suffering from SCD. Emotions and cognitive performances are measured prior to and following the immersive experience. Comparative analyses will establish the emotional progression and cognitive improvement.

Finally, the previous objectives will contribute to identifying if the following hypothesis is true: By increasing positive emotions and reducing negative emotions through the activation of the brain reward system (BRS), music improves cognitive functions in participants suffering from subjective cognitive decline (SCD).

1.3. Thesis Organization

The rest of the thesis is organized in eight chapters as follows.

- **Chapter 2. Alzheimer's Disease and the Benefits of VR** offers an overview of the disease, a review of the potential of VR as an intervention for AD and explores the importance of emotions in cognitive functions and well being.
- **Chapter 3. Therapeutic Environments** explores the two VEs, offering the supporting information for the creation of the environments as well as descriptions of the environments themselves.

- **Chapter 4. Experimentations** describe the experimental procedure for both environments.
- **Chapter 5. Results and Discussion** presents the results and offers a discussion with regards to both environments. This chapter also explores the concept, design and functionalities of a tool capable of reliably assessing cognitive state progress.
- **Chapter 6. Conclusions and Future Works** give an overview of the research project as a whole and explores potential research avenues for the progression of this research.

Finally, the appendices placed at the very end of this thesis offer additional information in relation to this research.

The works of this thesis, in collaboration with lab colleagues and colleagues from other departments and institutions, enabled to publish two conference papers (see appendices A and B) as well as a journal article (see appendix C). Another article has been submitted to the Annals of Physical and Rehabilitation Medicine but was rejected. Finally, a second journal article is currently underway, in which we analyse and compare the different virtual environments, including travel therapy and music therapy.

Chapter 2. Alzheimer's Disease and the Benefits of VR

2.1. Alzheimer's Disease Overview

Alzheimer's disease (AD) is the most common form of dementia. It affects behaviour, cognitive abilities as well as physical abilities. AD is often referred to as a disease of the memory, as its most notable symptom is memory impairment. Over 47 million people worldwide are suffering from this disease, and with the aging population, the importance of finding an effective treatment is becoming increasingly apparent. Several researchers have investigated the causes of AD and have revealed the extent of some neural damage in the disease. As the disease progresses, the accumulation of neural damage in key brain areas leads to deficits, ultimately affecting an individual's ability to perform activities of daily living (ADLs) [26]. While research has revealed much about the disease, there is still a long way to go to cure it.

AD is a neurodegenerative disease, that is, it causes a progressive loss of neuronal structure and function. The disease affects several regions of the brain, including the cortex, the limbic system and the hippocampus [26]. Since different brain regions specialize in different functions, a lesion will have a different impact depending on its location. The symptomatology of AD is therefore heterogeneous. There is a decline in cognitive and functional abilities, resulting in difficulties in decision-making, performance in ADLs, communication and memory. We also notice a decrease in the general interest and apathy. At the behavioural level, patients may exhibit unusual behaviours, such as hiding personal belongings and acting more abruptly. Finally, there is a progressive decline in physical abilities, affecting coordination, mobility and the ability to perform simple tasks such as feeding oneself [26].

2.1.1. Pathophysiology

On a physiological level, AD is characterized by two neuropathological lesions: Aβ plaques and NFTs. These lesions lead to synaptic dysfunction and brain atrophy. This section gives a brief overview of these abnormalities.

Aβ plates are clusters of extracellular proteins. Their toxicity stems from the fact that they can bind to several membrane receptors and, as a result, can activate several aberrant signaling pathways [27]. This leads to neurotoxicity and neurodegeneration of the affected regions.

There is also an accumulation of intracellular proteins: the NFTs. These are composed of tau proteins which have the role of stabilizing the cell's cytoskeleton [28]. It is proposed that instability of the tau protein in individuals with AD can lead to excitotoxicity, eventually causing neuronal death [29].

Synaptic dysfunction is common in patients with AD. In the early stage of the disease, the number of synapses and dendritic spines in the cortex is reduced. In addition, Aβ plaques cause an inhibition of synaptic currents as well as a decrease in synaptic plasticity [30]. It is proposed that memory and learning problems in AD are caused by this synaptic dysfunction [31].

Finally, AD patients display important levels of brain atrophy. The most pronounced shrinkage is found in the hippocampus; however, atrophy is also found in other regions and structures such as the cortex, and amygdala and thalamus. Depending on the region, the degree of atrophy does not necessarily correlate with the severity of symptoms [32].

2.1.2. Stages of the disease

While the effects of the disease are heterogeneous, the progression of the disease remains relatively constant, following a series of stages. These are separated into six more-or-less specific stages, or four broader stages: early stage, middle stage, late stage and end of life [26]. The progression of AD is caused by an accumulation of neuronal damage that leads to synaptic dysfunction and neuronal death, which can begin to accumulate as early as 20 years prior to the onset of symptoms [33]. The speed at which the stages progress varies from one individual to another. The stages are characterized as follows.

In the preclinical stage, individuals experience subjective cognitive decline (SCD). Cognitive abilities are slightly diminished, but not enough to pose a functional problem in the individuals' life. While many people with SCD remain in the stage, these individuals are at higher risk of progressing towards AD. In the early stage, at the behavioural level, individuals experience memory loss, difficulty communicating and mood changes. During the middle stage, cognitive abilities are decreased. At this stage, patients require some assistance in their everyday tasks. It is often at this stage that the diagnosis is made. In the late stage of the disease, patients require constant assistance and are unable to take care of themselves [26]. At the end of life, death is often caused by infections – often pneumonia – since individuals are stationary and therefore more vulnerable [34].

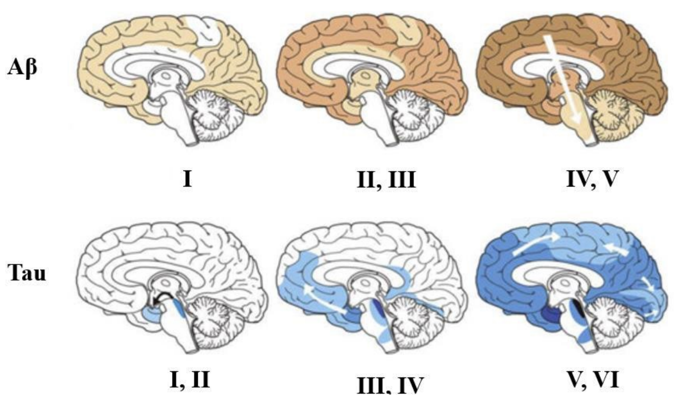

Figure 1. Stages of AD with according Aβ and tau protein progression. Retrieved from [35] with minor modifications.

2.2. Emotions in Alzheimer's Disease

While memories are critically impaired in AD, they are not necessary in order to experience emotions. Indeed, a study investigating affective states in people suffering from severe anterograde amnesia showed that after watching a short film, participants were happy or sad - depending on the film they were shown - but could not remember what had caused their emotions. These observations suggest that emotions persist regardless of memory of the event that caused them [23], [36]

A similar study examined the impact of memory deficits on the emotional responses of individuals with AD. Results suggested that emotions last longer than episodic memory; the type of memory most severely impaired in AD. In this study, researchers asked individuals with AD to watch short films specifically designed to elicit either positive or negative emotions. Results of the study showed that individuals who remembered less of the film tended to experience sadness for a longer period of time compared to those who had a better recollection of the movie. Of the two emotions that were studied, sadness tended to last longer than happiness. Moreover, as for people suffering from anterograde amnesia, emotions lasted longer than the memory of the films for both the positive and negative short films in people with AD [37].

When it comes to people suffering from AD, emotional states are altered, whether it be by failing to recognise emotions or to experience them at all. Individuals with AD experience seemingly less intense emotions than before the onset of the disease. One research group wondered whether this decrease in intensity was caused by a lack of understanding of the events. Results showed that even when patients understood the events as much as the control group, their emotions concerning the events were less intense. This decrease in intensity was observed for both positive and negative emotions. The origin of this loss of intensity is unclear. Some research suggests it might be the result of a degradation or loss of control of the region of the brain responsible for experiencing emotions, or perhaps a degradation of an important neurotransmitter in emotions [38].

Finally, one important and common emotional change n AD is apathy. Indeed, many individuals suffering from the disease become noticeably apathetic. This lack of motivation and emotion has been related to diminished wellbeing and increased morbidity [39].

2.3. The Potential of Virtual Reality

2.3.1. Overview of Virtual Reality

VR can be seen as a simulated experience. We distinguish immersive versus non-immersive VR by the following: immersive VR requires the use of a head-mounted display, while non-immersive VR does not. Non-immersive VR refers to environments displayed the traditional way: on a television or computer monitor. For simplicity, the term VR in this thesis will refer to immersive VR unless specified otherwise.

Over the last few years, VR has been popularized in a number of fields in addition to its entertainment purpose. VR requires a head-mounted display, which enables its users to experience a visual and sometimes auditory sense of *presence* in a VE. Some environments require users to manipulate the environment, while others are completely passive. A key element which makes VR so interesting and widespread is its remarkable ability to create full immersion. Indeed, VR tricks the mind of users, increasing the sense of presence in the VE, bringing the experience closer to that of real life [40].

The main advantage of VR compared to other interactive environments is that it isolates users from external visual distractions. We refer to this as *immersiveness*, which can be defined as "a VR system's functional capabilities, including field of view, hardware specifications, level of interactivity with VEs, and the extent to which the user is isolated from the outside world" [41]. Many factors contribute to immersiveness of a VE, with the field of view being a major contributor. A field of view similar to that of humans increases the sense of presence, giving a more realistic experience [41].

VR technology has been applied in a variety of different fields, with notable results observed in the psychological realm. Indeed, VR has been used to treat various disorders, including brain damage [42], anxiety disorders [43] and alleviation of fear [44]. Interestingly, VR has also shown to be helpful in the rehabilitation of cognitive functions [45].

2.3.2. Uses of VR for Alzheimer's Disease

Until recently, few studies investigating non-invasive treatments for Alzheimer's Disease made use of VR, while a larger proportion made use of non-immersive VR. There have been many reports revealing the benefits of using VR with AD patients. The dynamic, multisensory and interactive aspect of VR allows for a strong ecological validity [46]. There is some indication that VR interventions with computerized cognitive training can improve cognitive domains in individuals with mild cognitive impairment (MCI) or AD [47], [48]. Moreover, participants prefer completing cognitive training tasks in VR over its pencil-paper counterpart [49]. Interestingly, it is proposed that a more engaging training will be more effective, which could make a significant difference in efficacy between VR and non-VR exercises.

In addition to its uses for psychological and cognitive states, interesting new research is now investigating the power of VR at a more physiological level [50], [51]. For instance, immersion in a VE may alter synaptic activity in such a way as to affect interstitial Aβ levels [52] leading to tangible behavioral and cognitive benefits.

Chapter 3. Therapeutic Environments

This chapter explores the two virtual environments we designed. The first environment immerses its participants into a train, giving the impression of traveling from one place to another passing by scenic locations. The second environment immerses the participant into a theatre where they can enjoy a selection of songs paired with colorful scenes. Both environments were created to encourage positive changes on affective and cognitive states.

3.1. Therapeutic Train Environment

3.1.1. Underlying Theories

Hodophilia: One's love for travel. Wanderlust: One's desire for travel. There are many words in many languages which describe the feelings you get from traveling. From the Swedish word *resferber* which means "the restless race of the traveler's heart before the journey begins", to the German word *fernweh* which refers to "the feeling of being homesick for a place you've never been; a crave for travel" [53], language alone shows how travel can be filled with intense emotional reactions. Keeping in mind that emotions play a major role in AD, travel seems to be a promising place to start our research, and we were not alone to think so.

A group of researchers investigated how simulating a travel experience for people with AD could affect their day to day lives [54]. In their study, the researchers designed two physical versions of a fictitious train in a retirement home. To make the experience seemed more genuine, participants were asked to "book their travel" by buying a ticket at the fake ticket office, and to wait at the "train station" for the train to arrive. Again, this is all fictious. A ticket office, a train station and a train car were recreated within the residence. Upon its "arrival", participants would enter the train, take a seat and travel to the next station for a maximum time of 30 minutes.

Two different train prototypes were created: one basic and the other more thought-out and realistic. To enter the more basic prototype, participants opened two wooden doors which led to a room representing the interior of a train wagon. The wagon contained two armchairs, a table, and a lamp. The windows were simulated by LCD screens displaying the scenery change captured by video taken from a real train. The second, more realistic prototype, was created by a team consisting of the research group, an architect, and therapists. This version of the train was isolated from the rest of the residence and the visual elements resembled more closely that of a train. Similar to the first prototype, the windows of this prototype were represented by screen giving the illusion of travel.

Figure 2. Biamonti's basic train prototype.

Figure 3. Biamonti's realistic train prototype.

The experience investigating the impact of the first, most basic prototype, was tested on 20 participants. No positive results were obtained. Contrarily, the second prototype revealed interesting and positive results. While testing on 37 individuals, 31 participants claimed they felt as though they were in a train, while none had claimed so for the first prototype. Results of the study showed that wandering and agitation, both common symptoms of AD, were reduced (see pages 285-299 of the proceedings of the what's on: cumulus spring conference [54]). On a more psychological level, participants showed improved anxiety, apathy and sleep [54].

Due to the fact that travel is an emotionally powerful experience, and that a Biamonti's study has shown benefits for simulated travel in people with AD, we believe it is a promising avenue to explore, and even more so by pairing it with VR. In comparison to Biamonti's study, our study focuses on the emotional and cognitive changes brought on by the immersive experience, such as changes in affective state, attention and memory functions, as opposed to behavioral disorders, agitation and aggressiveness. Furthermore, a big difference with Biamonti's experiment is that our environment is fully immersive, entailing that the user can freely turn there head in 360 degrees instead of simply looking at a screen.

3.1.2. Environment Description

Based on Biamonti's environment, we created a VE which would immerse the participant in a virtual train traveling in various environments. Using VR for this experience is highly beneficial in the sense that it requires no major changes within the residence. Furthermore, the experience is more easily replicable in a number of residential homes and can be utilized by more than one person at a time if residents have more than one headset. In addition, this experience can be much more immersive than Biamonti's experiment, as the participant is, in a sense, isolated from the external world. This is a key element when trying to reduce stress and other negative emotions.

The game engine Unity 3D and its built-in physics engine were used to create the environment. The environment consists of a train traveling within different sceneries. The participant is seated in a window seat, near a happy family with two children. The interior of the train replicates that of a real train (see figure 4).

Figure 4. Screen capture of the train therapy environment. The interior of the train is well lit, and a family is sitting close by.

Figure 5. Screen captures of the train therapy environment. This is the second external environment with the wintery scenery.

While looking outside the window, participants can observe the changing scenery. The first outdoor environment consists of a forest with passive animals close by. When the train passes through a tunnel, the participant emerges from the other side in a different environment: this time a snowy environment with large mountains, similar to the alps. Animals can also be observed in this scenery. Finally, when the train passes though the second tunnel, the participant emerges in a sunny desertic environment

3.1.3. Component Choices

In the designing of the environment, the different components were carefully chosen in order to attain specific goals. More specifically, aspects such as transportation method, travel locations, ambient noise, lighting, and visual elements were purposefully chosen. This section describes the components and their intent.

Firstly, the transportation method selected was the train. This decision was made because a study has already shown that travel through a virtual train could be beneficial for AD patients. Furthermore, trains are well known to allow for a beautiful view of the scenery outside. On the contrary, a plane would not permit such diverse et visible scenery and can often be a source of stress. As opposed to a car, a train is more closely tied to a sensation of travel, which may generate a more pleasurable sensation.

Secondly, three different travel locations were selected: a forest, snowy mountains and a desert. A set of three sceneries was chosen as opposed to one single scene in an attempt to reach a broader population. While people may love the snow, others may not. Moreover, different sceneries can provide more opportunity for the participants to relate to at least one of the environments. In general, something familiar is perceived as more enjoyable [55] and including more than one environment increases the potential of generating a sense of familiarity.

Thirdly, the ambient noise and lighting of the environment were chosen to provoke a neutral to positive experience. There is a constant sound of train accompanied by a smooth and cheerful melody. The lighting is bright, which suggests a beautiful day. Better lighting tends to be associated with a greater sense of security [56], and it is important that the participant feels secure in order to appreciate the experience.

Finally, visual elements such as a family inside the train and passive animals outside were placed. Putting a family in the train was meant to make the environment seem less hostile. The animals outside offer something to focus on other than just the scenery.

3.1.4. Contributions

The work presented in chapters 3 was published in December of 2019 at the 9th International Conference on Sensor Networks, by the following authors: Abdessalem, Byrns, Cuesta, Manera, Robert, Bruneau, Belleville and Frasson. The paper received the Best Paper Award.

Contributions to the paper are specified in appendix A.

Now that we have discussed the first, simpler VE, we continue this section with an exploration of the second, more complex and intelligent VE: The Music Therapy environment.

3.2. Music Therapy Environment

3.2.1. Underlying Theories

We have all experienced it: an emotional shift, shivers down your spine or the swaying of your head while listening to music, and the science is there to back it. Music can easily trigger strong emotional responses, and sometimes even involuntary physical responses such as moving to the beat [57]–[59]. It comes as no surprise that, despite having no evolutionary advantage, music has been a part of human experiences for decades. Perhaps this is due to the psychological effects of music, or even it’s neurological effects.

Music therapy (MT) provokes noticeable changes in psychological and behavioral states of people with AD. Studies have shown increased states of happiness and reduced stress following MT sessions [60]. Furthermore, other unwanted symptoms of the disease, such as agitation, stress and depression are improved following a MT session [23], [25], [61], [62]. Overall, research shows increased wellbeing in people with AD as well as improved relations with their caregivers.

In addition, studies have also underlined music’s potential for neurological rehabilitation. Reports show slowed cognitive decline [63], improved memory, improved orientation, reduced stress, as well as improved behavioral and psychological states [23] following MT sessions. On a cognitive level, some studies propose that music could potentially enhance cognition and memory [23], [64]. It is possible that the brain reward system (BRS) plays a role in music’s enhancement of certain cognitive functions.

3.2.1.1 Involvement of the Brain Reward System

The brain reward system (BRS) is a network of brain structures which are activated as a result of rewarding or reinforcing stimuli. The exposure to such a stimulus activates the reward system through an increased release of the dopamine neurotransmitter, consequently generating the rewarding feeling [65]. These stimuli can be anything associated with a positive, enjoyable experience. Common examples of these are food, sex, drugs, and music.

The BRS is important for the processing of **emotional stimuli** and some **memory** functions. Famous studies investigating the repercussions of lesions of the amygdala, a key structure in the BRS, have revealed that such damage causes implicit memory impairments [66]. Implicit memory is a type of memory responsible for the storage of unconsciously acquired knowledge such as riding a bike and brushing your teeth. It is now established that lesions of the amygdala can have detrimental effects, such as impairments in the **unconscious** recollection of perceptual and motor skills [67]. It follows that the reward system plays a certain role in implicit memory recall.

It has been shown that activation of the BRS by music maximizes pleasure by increasing the activation of specific brain structures and decreasing the activation of structures associated with negative emotions through an inhibitory mechanism [68]. Furthermore, the reward system plays a role in cognitive state, in addition to affective state. For example, short exposure to a rewarding stimulus can cause physiological changes which promote better problem-solving performances in stressful situations [69].

3.2.2. Environment Description

The environment was created using the Unity 3D game engine. The location of the environment is a traditional music theatre, where the participant is seated in the audience. The theatre is composed of warm colors, with classic red seats for the audience and a cliché red curtain on the stage, opening and closing for each scene.

The course of the experiment goes as follows. Eight song excerpts, lasting 30 seconds each, are sequentially presented on stage. Each song is clearly separated from the previous by the curtains closing the scene and opening for the next song. As the curtains open, instruments corresponding to those used for the song are revealed on stage. The instruments are lightly animated to move along with the music.

Behind the instruments, participants can observe firework-like visual effects, called particles, of various colors. These particles are synchronized with the music and move as a function of its intensity. In a sense, it is as if the participant is observing the music. Different particle effects appear for each song, varying either according to their colors or movement patterns.

Following the presentation of the eight song excerpts, the environment is adapted to the participant. The environment uses its intelligent agent to identify the most beneficial song among the eight that were previously played according to the emotional response recorded by an EEG headset. Once identified, the intelligent agent adapts the environment and presents the most beneficial song to the participant for the remainder of the experimental session.

Figure 6. Screenshot of music therapy environment, scene for Clair de Lune by Debussy.

Figure 7. Screenshot of music therapy environment, scene for La Vie En Rose by Edith Piaf.

3.2.3. Neurofeedback agent

In order to adapt the VE to each person, we created a neurofeedback intelligent agent capable of recording and analyzing the users' emotions using Emotiv EEG headset data in real-time. The integration of this agent was made possible by Hamdi Ben Abdessalem, who created it and implemented it within the environment.

To appropriately adapt the environment, the agent analyses the emotional impact each of the eight songs have on the participant, and, for each song, calculates a score based on the measured emotions and mental states. The lower the negative emotions are, the higher the score. Following the presentation of the eight song excerpts, the agent selects the song with the highest score for the current participant. In other words, the agent selects the song that has the most positive impact on the person's emotions. The agent will then adapt the VE by playing the selected song again, this time for a longer period of time. This real-time adaptative system using neurofeedback allows the creation of a personalized-MT without the need of the participant's explicit input.

3.2.4. Component Choices

Each component of the environment was carefully chosen. This section justifies the choices made for the location, the music and the visual elements.

One of the first decisions to make was the general idea of the environment: where would it take place? Music therapy generally takes place in a location with nothing very particular about it other than space, chairs and instruments. The intervention could have taken place in a virtual living room, a virtual park and a virtual music classroom, for example. We decided to settle on a theater, where special events usually take place, such as plays, orchestra performances and comedy shows. By choosing a theater, the environment itself gives the impression that something special is going to happen. It can trigger emotions like happiness, curiosity, and excitement.

In terms of the songs, multiple facts and theories were at the foundation of their selection. A portion of the songs was selected because they contained melodies with structural features associated with anxiety reduction (i.e. slow tempo, low pitches) [70]. These songs had as a purpose to induce a soothing and/or relaxing feeling. The other portion of the songs was selected as a function of their popularity. Sihvonen and colleagues propose that listening to known music can have positive effects for neurological rehabilitation, including the stimulation of autobiographical memories that can provide a sense of identity [71]. This hypothesis is supported by several studies. In this train of thought, some songs were selected because they had reached the billboard top 100 hits charts during the years corresponding to the participant's reminiscence bump. The reminiscence bump refers to a time period where events and memories are more likely to be remembered. This time period corresponds to ages 10 to 30, with a maximum likelihood peaking around 20 years old [72]. With the mean age of our participants estimated to be around 70, a number of songs were selected because they reached the billboard charts between the years 1960 and 1980. Furthermore, seven out of the eight songs were released prior to 1970, increasing the chances of being recognized by the participant. Table I shows more specifications about the song selection and the reasons for them.

On the stage there are instruments and waves of colors moving to the rhythm of the music. The choice of the colors of the wave particles is based on the purpose of the songs: songs with a relaxing purpose have colors in shades of purple-blue and yellow-red. Songs with a calming purpose will have colors in the shades of blue, blue-green, green, reddish-purple, purple, and purple-blue. Finally, songs with the purpose of stimulating will have colors in the shades of green-yellow, blue-green and green [73].

Table I. List of songs and reasons of choice.

Artist / Title	Type	Instrument(s)	Goal	Color shades	Release year	Billboard Year
Franz Schubert /**Ave Maria**	Popular, calm	Piano	Relaxing	Purple, Blue	1825	N/A
Mozart / **Allegro**	Popular, fast rhythm, classical	Violins	Stimulating	Purple, Pink, Orange, Yellow	1756-1791	N/A
Bensound / **Ukulele**	Jovial	Acoustic guitar maracas, drums, xylophone	Soothing	Purple, Blue, Red, Orange, Yellow	2018	N/A
Claude Debussy / **Clair de lune**	Popular, classical	Piano	Relaxing	Purple, Blue, Red	1905	N/A
Edith Piaf / **La vie en rose**	Popular	Trombone, drums, microphone, violins	Stimulating	Blue, Green, Yellow, Red	1947	1950, 1977
Buddy Holly / **Everyday**	Popular	Xylophone, micro, bass	Soothing, Stimulating	Purple, Blue, Green	1957	1957
Ritchie Valens / **La Bamba**	Popular, fast rhythm	Electric guitars maracas, microphone, drums	Stimulating	Blue, Green, Yellow	1958	1959
Louis Armstrong / **What a Wonderful World**	Popular, calm	Violins, electric guitar, microphone	Relaxing	Purple, Blue	1967	1988

3.2.5. Contributions

The work presented in section 3.2 results in two publications (see Annexe B and C). The first paper was published in June of 2020 at the 16th International Conference on Intelligent Tutoring Systems. The second paper was published in August of 2020 in the Journal of Biomedical Science and Engineering. The authors of both papers are the following: Byrns, Abdessalem, Cuesta, Bruneau, Belleville and Frasson. Contributions to the papers are specified in Appendices B and C.

Now that we have explored the two virtual environments involved in this research project, the following section takes a look at the project's experimental procedure.

Chapter 4. Experimentations

In this chapter, we explore the experimental procedure. We start by introducing the eligibility criteria to take part in the experiments. We briefly present the required equipment and go on to explore the different steps of the experimental procedure and describe six cognitive exercises, key to the measurement of cognitive improvements. We end this chapter with a small section on the measurement of emotions though EEG recordings, and how brain lateralization and neuronal activity enable us to determine emotions in real time.

The experimentations of both environments relied heavily on the contribution of Hamdi Ben Abdessalem and Marwa Boukadida.

4.1. Study population

Participants of the study were recruited by the Institut Universitaire de Gériatrie de Montréal (IUGM) staff.

For the train environment, 19 eligible participants were recruited. Of these, 11 participants were women and 8 were men. The mean age of the group was of 69.68 (SD = 5.49). Similarly, 19 participants took part in the music environment. This group had a higher mean age, being of 72.26 (SD = 5.82), and was composed of 13 women and 6 men.

To be eligible, applicants had to meet the following criteria:

- Over 60 years old
- Speak French
- Normal or corrected-to-normal vision
- Normal hearing
- Meet the criteria for SCD:
    - Self-assessment of worsened memory
    - MoCA score between 20 and 30
    - No logical memory impairment

4.2. Characteristics of the Experiments

4.2.1. Experimental Procedure

In the pre-experimental session, research candidates who met the eligibility criteria were asked to sign a consent form and return for the experimental session at an agreed upon date.

In the following session, participants were asked to complete the experiment. Upon their arrival, participants were asked to fill out the pre-experiment forms. Once filled out, an EEG headset was equipped on the participants head, and they were asked to solve a series of 3 attention and 3 memory exercises. Once completed, participants were equipped with the VR headset and immersed in the VE: the virtual train for the train therapy experiment, and the virtual theater for the music therapy experiment. The immersive experience lasted for approximately 10 minutes. Following the VE, participants were asked to complete variants of the same cognitive exercises, and finally complete the post-session forms. Throughout the entire experience, careful attention was paid to the electrode's statuses to ensure a good signal. Figure 8 shows the experimental procedure.

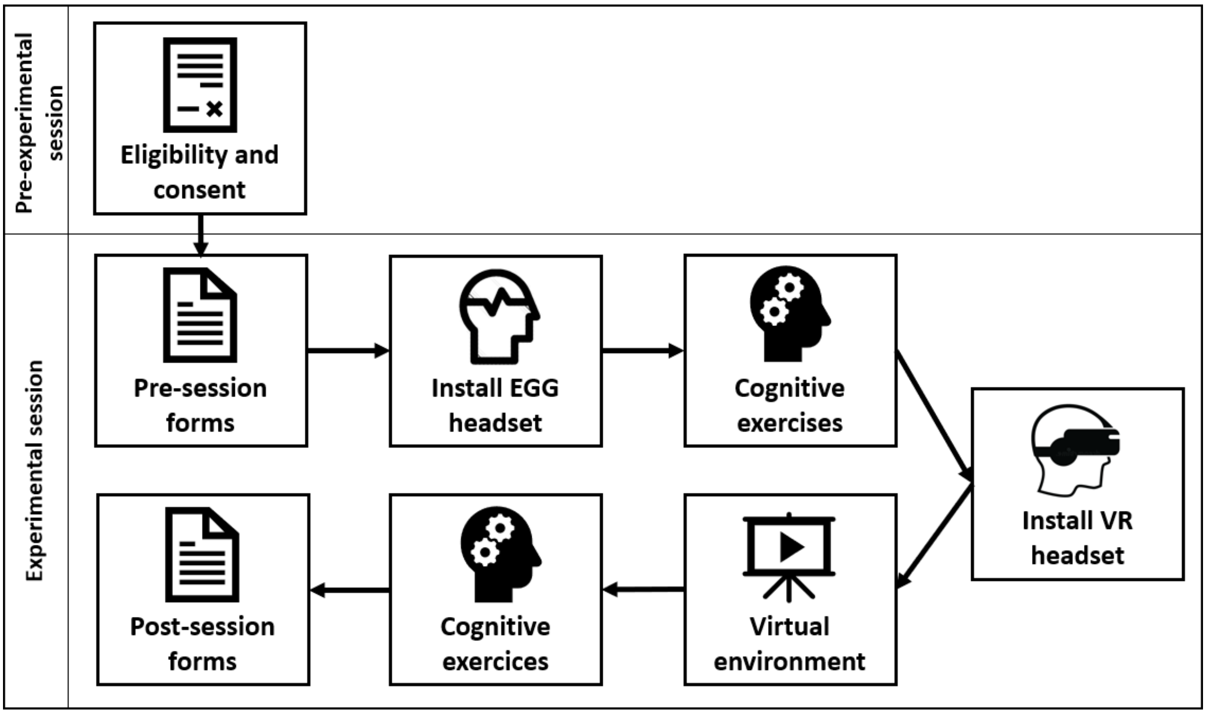

Figure 8. Experimental procedure.

To verify the results, a control group composed of candidates meeting the same requirements as those participating in the virtual immersion will undergo the same experimental procedure but will not be immersed in the virtual train nor the virtual music theatre. Indeed, this control group will perform the same cognitive exercises before and after the virtual environment, but the environment will consist of nothing more than a gray screen. This will help demonstrate the effect of our intervention while taking into consideration factors other than the virtual environments themselves. Due to the limited number of participants as well as financial reasons, experiments were first conducted without control group to verify the protocol's potential. Future lab work will repeat these experiments on a control group to further confirm results.

In terms of equipment, the participants were equipped with two separate headsets. The first headset, which was used to record the participant's brain activity, and consequently their emotional states, was the Emotiv Epoc EEG headset (see figure 9). The headset works by recording activity in specific brain regions thanks to its strategically placed electrodes. The second headset was the Fove 0 VR headset, which was used to immerse participants in the VE (see figure 7). The participant's immersive experience was induced by the visual and auditory stimuli, recreating the Train or Music environment, generated by the headset.

Figure 9. Experimental equipment.

4.2.2. Emotion detection and recognition

To detect and recognize emotions in real time, we used the Emotiv Epoc + headset. The headset's fourteen electrodes are strategically placed on the participants head, as shown in figure 10. These regions correspond to antero-frontal, fronto-central, parietal, temporal and occipital regions. These regions are important since different emotions evoke spatially distinct brain activity. By brain activity, we mean the activation of a specific network of neurons. The activation of neurons causes local changes in voltage which can be detected by EEG. These electrical pulses can be recorded as brain oscillations of different frequencies, varying between delta (0.5-4 Hz) to gamma (30-40 Hz) such as alpha and beta. Due to the lateralization of the brain, which results in different brain regions having distinct functions, analysis of the EEG readings can provide insight as to what this activity represents. Due to this principal, the pairing of an EEG system with another system capable analyzing the EEG data enables to see the specific emotions felt by the participant. This is precisely what the Emotiv Epoc + EEG headset technology does (see figure 10). Ultimately, the system's algorithms enable us to measure the following five mental states: meditation, frustration, engagement, excitement and valence. In our research, we focus primarily on frustration and valence, where valence is a value between -1 and 1 which indicates whether the individual is in a more negative (-1) or positive (1) emotional state.

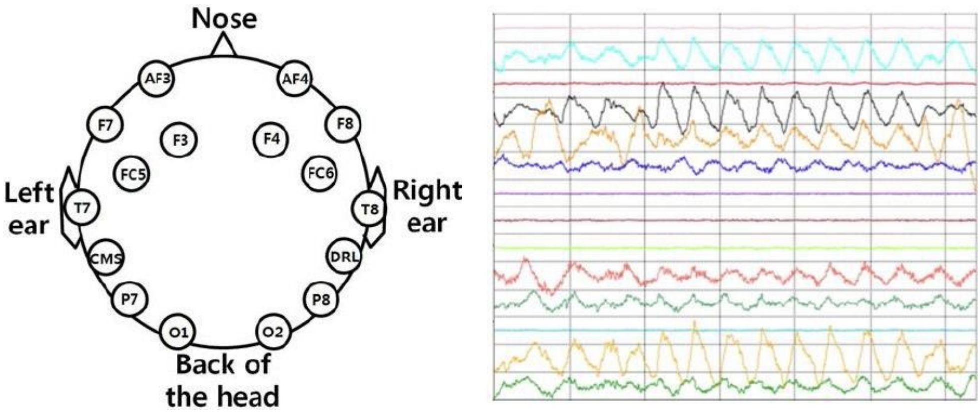

Figure 10. Emotiv headset electrode locations and example of data collection [74].

4.2.3. Cognitive exercises

The goal of our experiments is to determine the affective and cognitive impacts of the VEs. To measure the affective state, the EEG headset monitors brain activity and records changes in emotional states. To measure the cognitive impact, on the other hand, we measure the participant's performance in a series of carefully selected cognitive tasks targeting key brain functions. In the case of this research, we targeted attention and memory skills. This section briefly describes each of these exercises.

4.2.3.1 Attention tasks

For the first attention task, participants are asked to listen to and memorize a sequence of numbers. They are then asked to repeat the sequence in the correct order, and then repeat the sequence once more but in reverse order. Figure 11 shows an example of the numerical pad on which the participant must repeat the sequence.

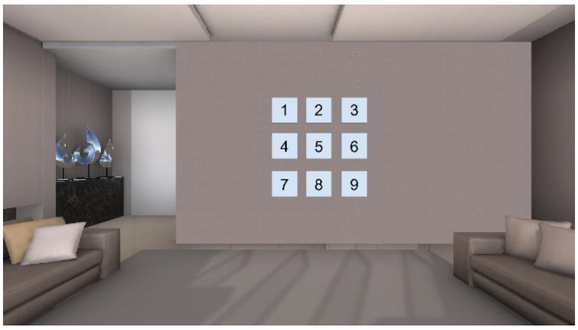

Figure 11. First attention task screen capture (Task 1).

During the second attention task, participants are asked to listen to a voice saying random letters and to press the space bar key rapidly after hearing the letter ‘A’. This is a selective attention task.

Finally, for the third and last attention task, participants are presented with the image of an item for a short period of time. Then, four options, each containing one distinct letter, appear on screen, and the participant must identify the first letter of the item they have just been presented with. Figure 12 shows an example of this exercise. In this case, since the image is of a chair, the correct answer is the letter ‘c’.

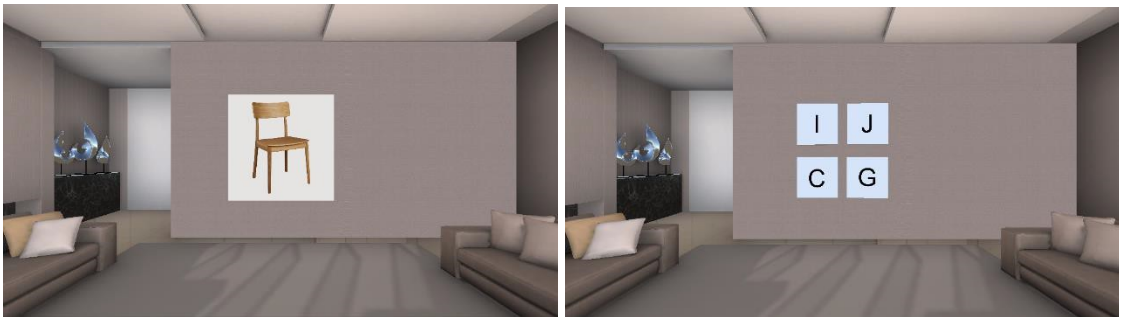

Figure 12. Third attention task screen capture (Task 3).

4.2.3.2 Memory tasks

For the first memory task (forth overall task), participants are asked to memorize a series of objects presented visually or orally with their name. They are then presented a series of object images or words either visually or auditorily. Participants are asked to determine whether the object was seen visually, auditorily or never presented. Figure 13 shows an example where the word or the image place was never presented.

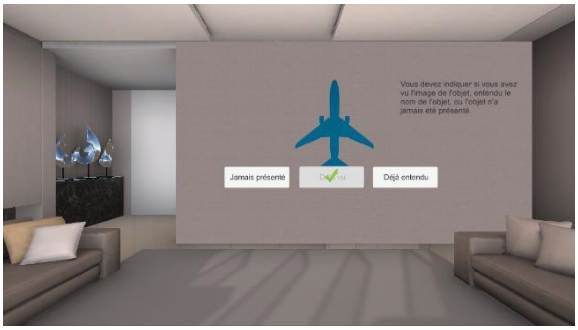

Figure 13. First memory task screen capture (Task 4).

For the second memory task (fifth overall task), participants are presented with a sequence circles, which is highlighted in a specific order. The participant is asked to memorize and reproduce the same sequence. Figure 14 shows that circles' random positions, with the yellow circle being the highlighted one.

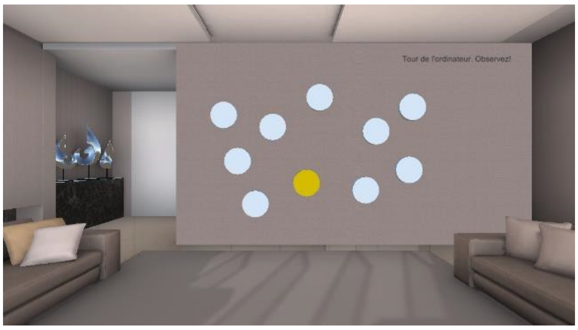

Figure 14. Second memory task screen capture (Task 5).

Finally, for the last task (third memory task, sixth overall task), participants are asked to memorize a set of three pictures for a short period of time. The set is removed and then four sets of three pictures are presented, and the participant is asked to select the set which corresponds to the one they saw. Figure 15 shows an example of this task, where the correct answer is the bottom left.

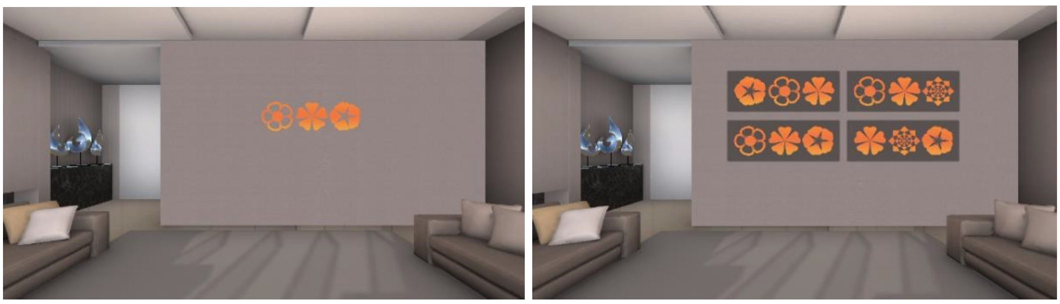

Figure 15. Third memory task screen capture (Task 6).

This chapter explored the experiment in its entirety: from eligibility criteria for the participants, the methodological steps of the experimental session to some explanations as to why certain equipments were used. The next section details and discusses the experiments’ results.

Chapter 5. Results and Discussion

Results of both the Train and Music experiments are detailed in this section. Here, we view how both environments performed and confirm or reject our two hypotheses; (1) can the environment improve affective state, and (2) can the environment improve cognitive state. Both environments obtained results which were published in various conferences and a journal. See the appendices for additional information concerning the publications.

The results analysis relied heavily on the contribution of Hamdi Ben Abdesslem.

5.1. Therapeutic Train Environment Results

The first objective of this experiment was to identify if it is possible to positively impact participants' emotions by reducing their negative emotions. With this in mind, we analysed EEG recordings of the participants emotions corresponding to times before, during and after the virtual travel. Results are presented in figure 16. Prior to the immersive experience, the mean frustration among the participants was 0.71, (minimum 0.41 and maximum 0.96). During the immersion, the mean frustration was of 0.51 (minimum 0.24 and maximum 0.94). Finally, the mean frustration after the immersion was of 0.53 (minimum 0.17 and maximum 0.79). Figure 16 offers a boxplot of the mean frustration levels throughout the experiment.

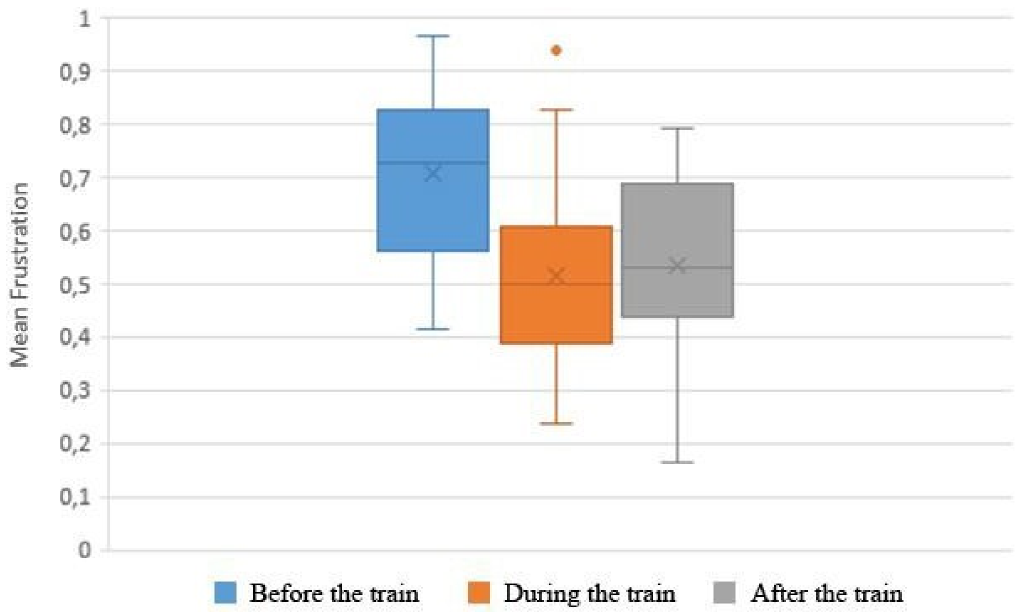

Figure 16. Boxplot of mean frustration throughout the train experiment.

Analysis of the individual frustration levels before, during and after the experiment are shown in figure 17. These results reveal that all but 2 participants (participant 9 and 12) experienced a decrease in frustration during the travel immersion.

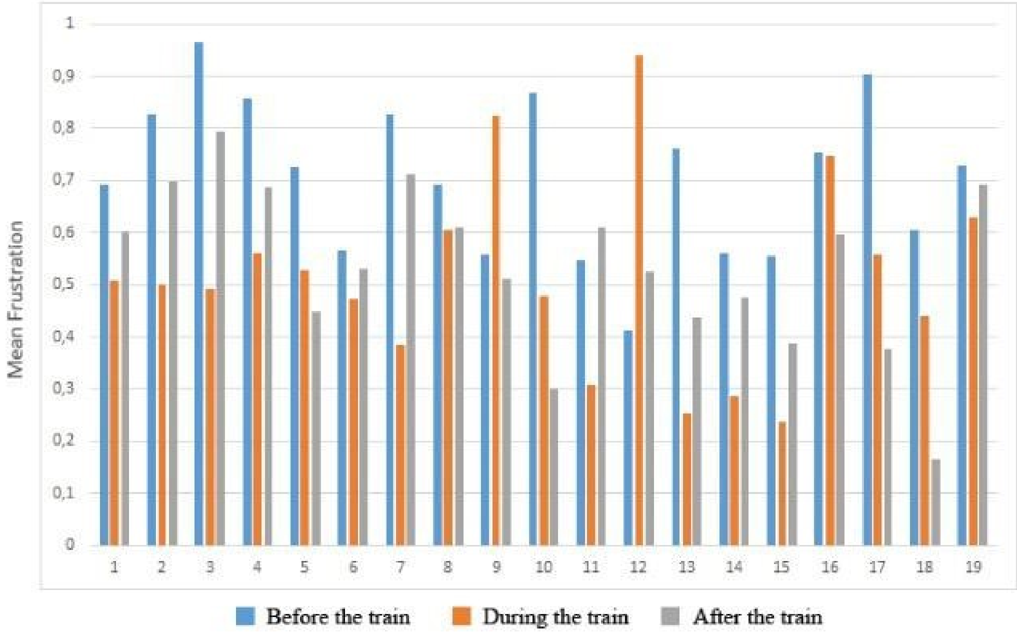

Figure 17. Histogram of individual frustration levels before, during and after the train immersion.

Results from the participants' self reports corroborate with the previous findings. Prior to the immersive experience, 31.6% of participants reported being stressed, while only 15.8% reported feeling stressed after the immersion.

This analysis led us to our second research question, namely, does the proposed system improve participants' cognitive functions? Analyses of the performances on all six cognitive exercise performances before and after the immersive experience helped reach our goal.

For the exercises targeting attention, minor results were obtained. For the first exercise, a negative mean improvement of 6.58% was observed. For the second exercise, a mean improvement of 0.48% was observed. Finally, a mean improvement of 7.02% was observed for the third attention exercise. Figure 18 shows the individual improvement results for each participant on all three attention exercises.

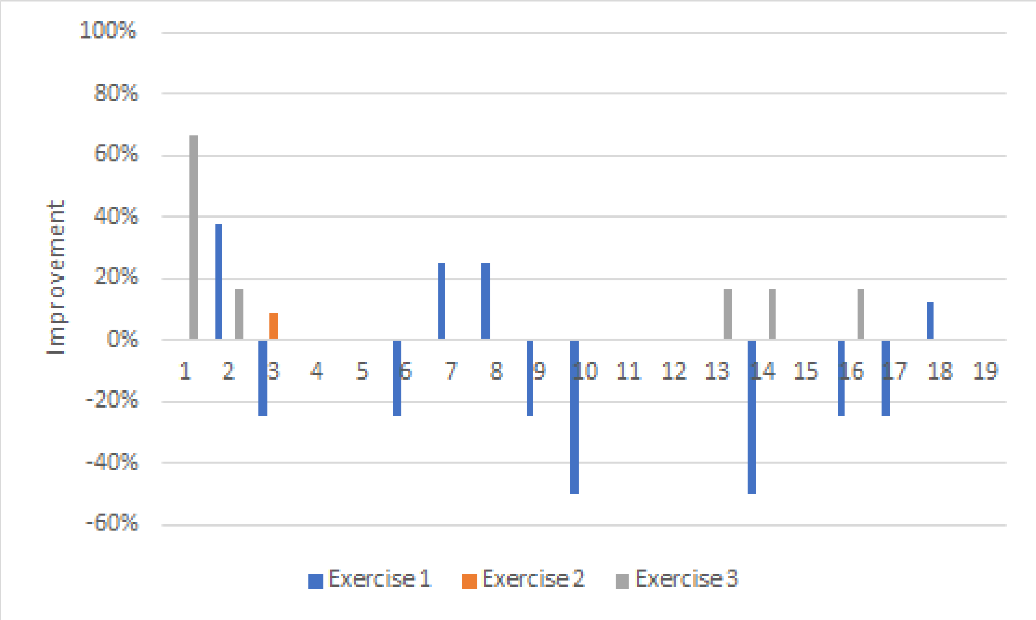

Figure 18. Individual performance improvements for attention exercises 1, 2 and 3 for train therapy intervention.

For the cognitive exercises targeting memory functions, higher, more conclusive improvement levels were observed. Participants showed a 10.53% mean performance improvement for the first memory exercise (exercise 4). For the second memory exercise (exercise 5), a mean performance improvement of 20% was observed. Finally, for the memory last exercise (exercise 6), we observed a mean performance improvement of 10.53%. Figure 19 shows the individual performance improvements for all participants on all three memory exercises.

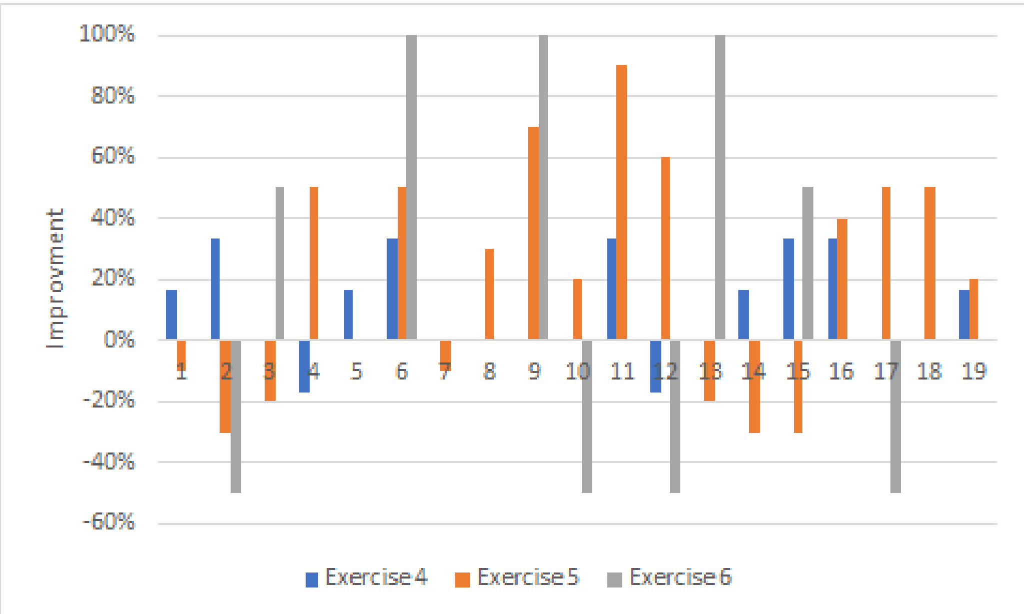

Figure 19. Individual performance improvements for memory exercises (exercises 4, 5 and 6) for train therapy intervention.

Our final analysis compared the improvement levels for the attention and the memory exercises. By grouping the attention and memory exercises into their separate groups and averaging the mean performance improvement for each participant for both exercise groups, results show a marked improvement for the memory exercises compared to the attention exercises. Figure 20 shows this difference.

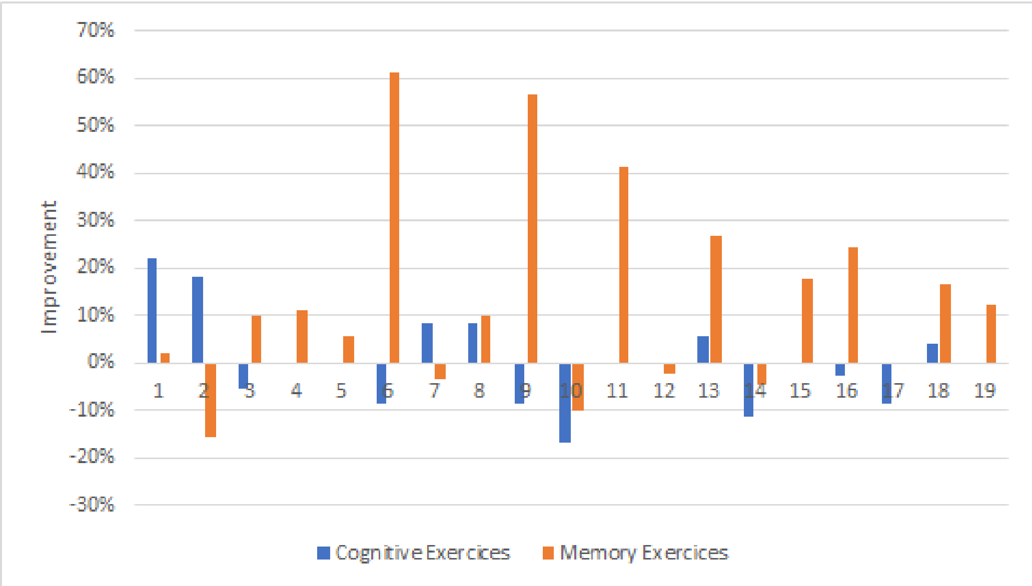

Figure 20. Performance improvement levels for all participants comparing the attention and memory exercises for train therapy intervention.

Results from our post-experience questionnaire showed that 73.7% of the participants found the virtual train relaxing, 89.5% of the participants reported enjoying the immersive effect, and 79% thought that the VR aspect of the experiment positively influenced their experience.

Now that we have looked over the results for the Train Therapy experiment, we continue this section with a description of the Music Therapy results.

5.2. Music Therapy Results

The first objective of this experiment was to identify whether or not virtual music therapy reduces negative emotions and increases positive emotions. To this end, EEG recordings corresponding to times before, during and after the immersion were recorded. Analyses of the level of frustration experienced by the participants revealed a tendency to towards a reduction in frustration. As shown on figure 21, frustration levels were generally higher before the intervention (mean: 0.69, minimum: 0.37, and maximum: 1.00), decreased significantly during the intervention (mean: 0.45, minimum: 0.21, and maximum: 0.82), and increased slightly following the immersion (mean: 0.51, minimum: 0.23, and maximum: 0.92).

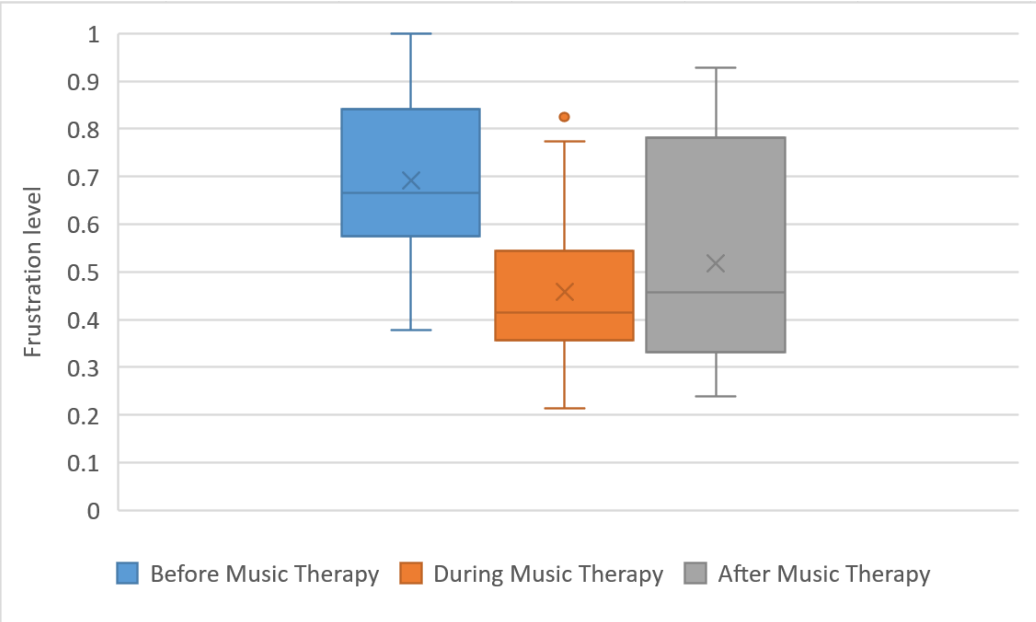

Figure 21. General mean frustration before, during and after the music therapy intervention.

In terms of the evolution of the positive emotions throughout the experiment, readings of valence showed a tendency for positive emotions to increase following the intervention. As shown on figure 22, the general mean valence before the intervention was 0.59 (minimum: 0.48, maximum: 0.78), then decreased slightly during the immersion (mean: 0.54, minimum: 0.47, maximum: 0.65), and finally increased substantially following the intervention (mean: 0.75, minimum: 0.55, maximum: 0.65).

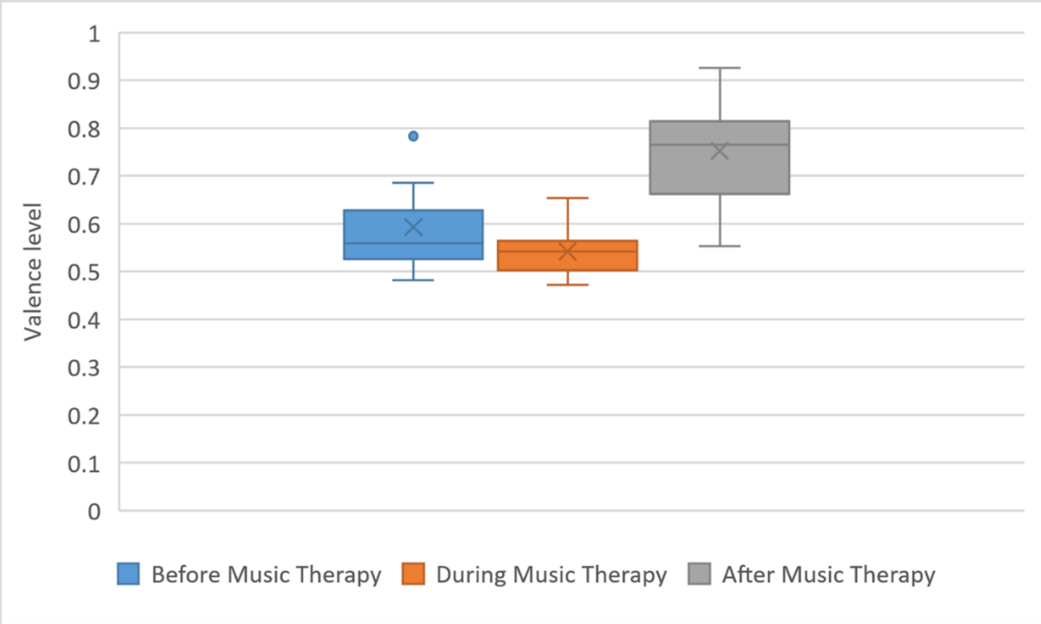

Figure 22. General mean valence before, during and after the music therapy intervention.

Our second research question asked whether the virtual music therapy experience increases cognitive functions or not. Results are separated into the two types of cognitive exercises: attention and memory.

Results show that attention performances are only slightly increased following the intervention. General mean improvements of 6.59%, 1.91% and 3.51% are observed for attention exercises 1, 2 and 3 respectively. Performance improvement levels are not consistent from participant to participant, nor is it from exercise to exercise. As shown in figure 23, for each exercise, some participants show a decreased performance following the, others show an unchanged performance, while others show increased performances.

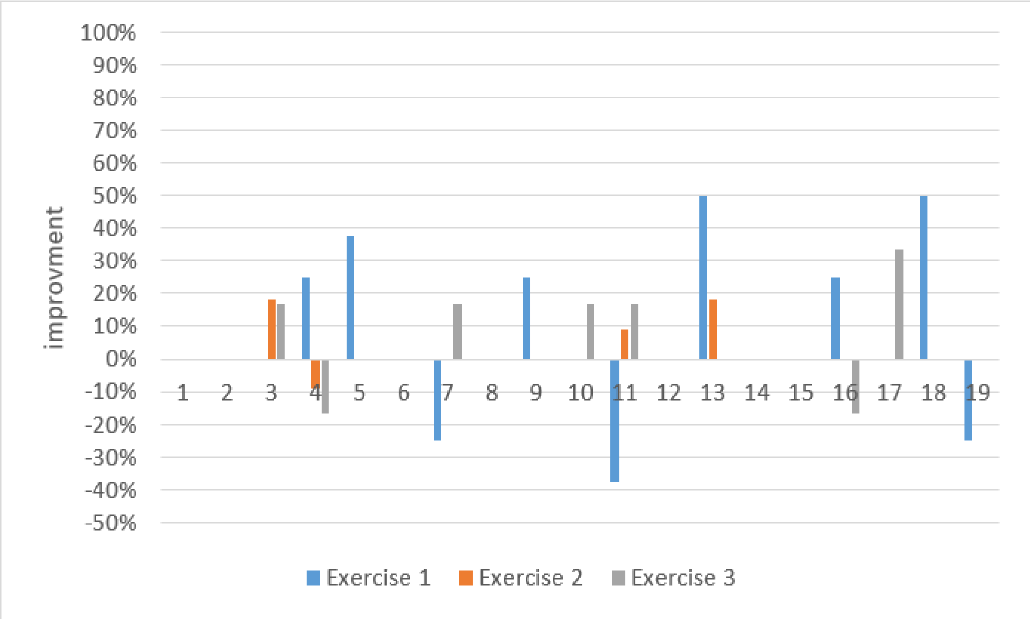

Figure 23. Individual performance improvements for attention exercises 1, 2 and 3 for music therapy intervention.

Results regarding the memory exercises show greater improvement levels. The fourth exercise (first memory exercise), fifth exercise (second memory exercise) and sixth exercise (third memory exercise) show improvements of 6.14%, 8.95% and 36.84% respectively. As shown in figure 24, similar to the attention exercises, performance increases were not observed for every participant nor in every exercise. However, unlike the attention exercises, the mean overall improvements are high.

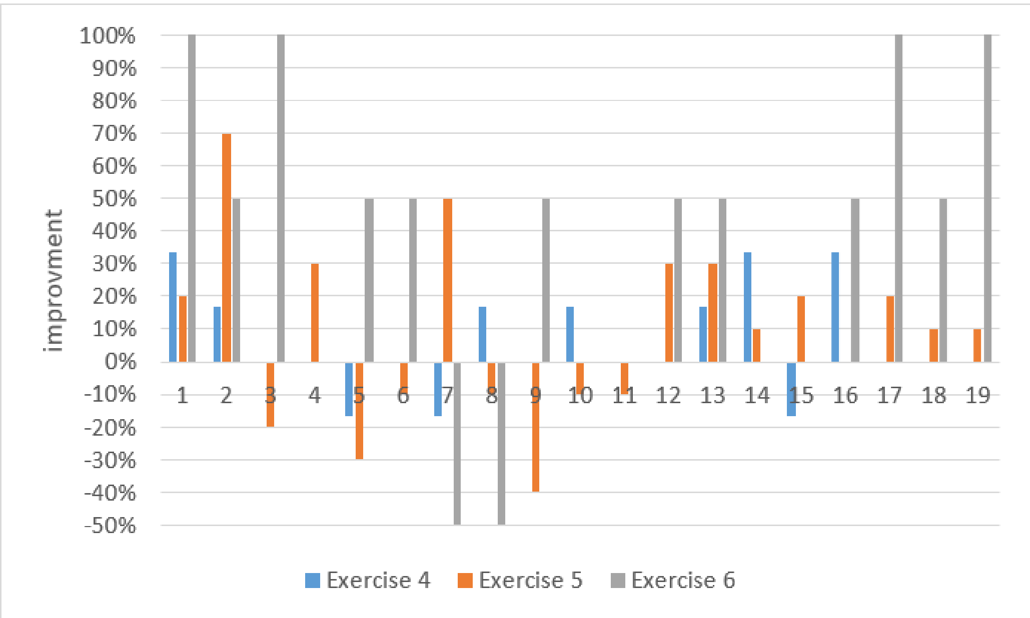

Figure 24. Individual performance improvements for memory exercises 1, 2 and 3 (exercises 4, 5, 6) for music therapy intervention.

Results from the post-session appreciation forms showed that most participants found the environment to be immersive, relaxing, and enjoyed the VR aspect of the experience. Table II gives a more detailed account of the results.

Table II. Post-session appreciation form responses.

Question	Yes	Neutral	No
Was the environment immersive?	89.5%	5.2%	5.3%
Was the environment relaxing?	89.5 %	5.2%	5.3%
Did VR positively influence your experience?	84.9%	9.8%	5.3%

Lastly, figure 25 shows a comparative analysis of the improvement levels for all three working memory tasks for both environments. Results show general mean improvements in for all three tasks.

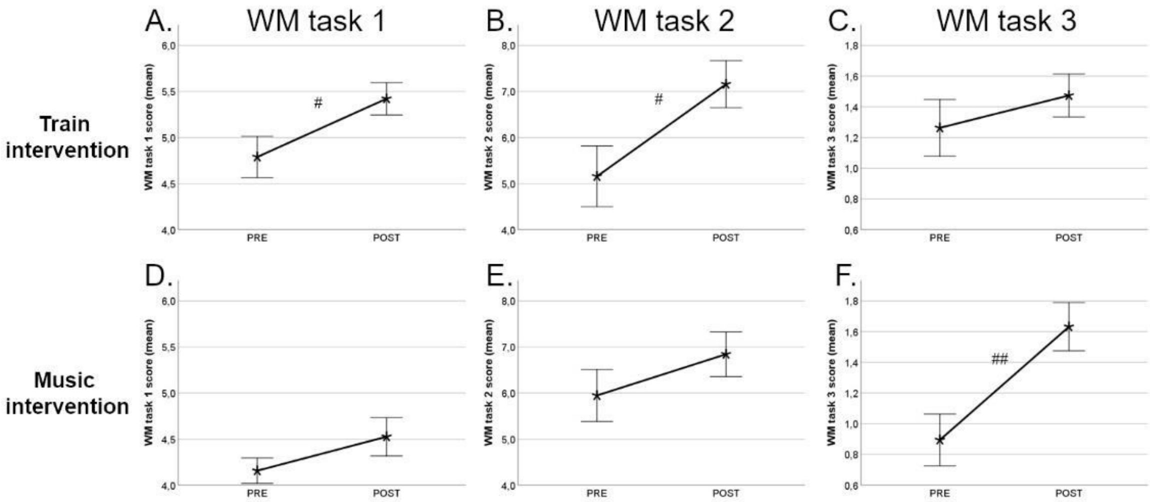

Figure 25. Memory task improvements for both virtual interventions. WM, working memory.

Overall, both interventions should an arguable increase in attention performances and a more concrete increase in memory performances. The following section discusses these results.

5.3. Discussion

For both environments, our objectives were the following: 1) Determine the intervention's impact on affective state, and 2) Determine if the intervention improves cognitive performance on attention and memory tasks. In this section, we review and interpret the results for both environments separately, and finish with a comparative discussion. We will first start with the train therapy environment.

In the train therapy experiment, participants were immersed in a virtual train traveling through three different sceneries. Participants were completely passive during the immersion and could see and hear various stimuli, such as animals and train track sounds, relevant to the environment. Our first objective asked what impact the environment would have on the participants emotional state. Results showed a decrease in frustration for most participants during the immersion. This improvement persisted beyond the duration of the immersion. Our second objective asked if the environment would improve the participants' cognitive functions. Among the six cognitive tasks, half tested attention skills, while the other half tested memory skills. Analysis of the attention task performances showed ambiguous results. Some participants improved, others decreased performance and others showed no difference. More conclusive results were observed for the memory tasks. Indeed, analysis of the memory task performances show a clear increase in memory performance.

Overall, the train environment showed optimistic results in terms of frustration reduction and memory improvement, and optimistic but less promising results in terms of attention improvement. In addition, our post-experiment questionnaire supported the measured improvement in emotional state, reporting that the train environment did, in fact, feel relaxing and reduce stress.

The second environment was slightly more complex than the first. For the music therapy experiment, participants were immersed in a virtual theatre and were shown a series of eight different songs. Using EEG recordings, an intelligent agent identified which song had the most positive effect on the participant's emotional state and selected this song to play at the end of the experimental session. This environment was therefore adapted to each participant according to their emotional response to the different elements, either visual or auditory, from the environment.

Our first objective asked if the environment could decrease negative emotions and increase positive emotions. Results based on the measurements of frustration and valence showed that the environment did in fact promote a more positive emotional state. Results further showed that this positive effect persisted following the intervention. Furthermore, post-intervention questionnaire results concorded with the emotion recordings: the majority of the participants enjoyed the intervention.

Interestingly, the EEG recordings showed a diminished valence during the intervention, and a substantial increase in valence following it. We believe this is due to the way the environment was constructed. During the general intervention, a total of eight different songs are shown. It is only at the very end of the intervention that the environment is adapted, and that the music played is the one evaluated as provoking the most positive emotional response. It follows that the emotional state at the very end of the intervention is best because it is optimized by the intelligent agent, which presents the song with the most positive effect on the participant at the end of the experiment.

These observations support the efficacy of the neurofeedback agent with regards to selecting the song which most suits the participant. Our goal was to increase positive emotions and decrease negative emotions, and this objective was accomplished. We believe the intelligent agent was successful in improving emotional state because our EEG recordings show just that: reduced frustration and increased valence. Furthermore, these positive changes – reduced negative emotions and increased positive emotions – where observed to a greater degree in the music intervention, possibly suggesting that a VE can indeed be intelligently adapted to improve affective state.

Our second research objective was to determine the effect of the intervention on cognitive functions. Comparisons of pre- and post-intervention cognitive task performances revealed a slight increase in attention abilities and a more substantial increase in memory function.

Our results lead us to believe that the increase in cognitive performance is due to the improved affective state induced by the music therapy environment. Despite not having any direct physiological measurement proving the causation from the affective state to the cognitive state, it has been repeatedly demonstrated that emotions and mental states are strongly correlated [75]. For instance, one study has revealed a tight relationship between frustration and workload: the higher the workload, the higher the frustration, with the reverse also being true.

Furthermore, memory task improvements were noticeably better than the attention task performances following the intervention. Readings have led us to put forth a theory giving reason for this occurrence. We propose that the larger improvement in memory task performances is due to a facilitated memory access generated by music. We explore this theory in greater detail in our article published in the Journal of Biomedical Science and Engineering (see annexe C). Let us recall that the amygdala, a structural part of the BRS, plays a key role in emotional processing and implicit memory. As proposed by a research group, emotional context associated with music and its saliency may lead to preserved residual memory functions in AD. They propose that since music is a salient emotional stimulus, it could potentially facilitate the access to the amygdala-based network and in turn provide better memory functioning [76]. This could explain why our participants experienced a small increase in attention performance and a larger increase in memory performance.

Our results show improvements in affective states and in some cognitive skills. While affective state analyses were based on EEG recordings, we recognize that cognitive improvement measurements were based on only six cognitive tasks. Although these tasks are variants of tasks which have repeatedly proven to give reliable results, our exercises only test six different cognitive skills among many others, and each exercise is carried out only once before and once after the intervention. A simple momentary lapse in attention could therefore drastically change the results of the experiment. To this end, we decided to create a complementary tool capable of assessing cognitive improvements with more precision and reliability. We describe this tool in the following section.

5.4. Cognitive Performance Improvement Measurement Tool

5.4.1. Introduction

The results of the train and music experiments relied heavily on the accuracy of the cognitive tasks before and after the intervention. The measurement tool used in these studies was based on exercises which have repeatedly shown to have little to no bias with regards to education, language and repetition is a tricky task. Despite these characteristics, our tool had a few flaws.

The cognitive performance measurement tool used in the train and music interventions was based on six cognitive exercises which have shown to reliably reflect the person's current cognitive state. The problem with our tool is that each exercise was repeated only once before and once after the immersive experience. This means that one single moment of inattention or confusion could completely alter the results. For these exercises accurately represent the participant's cognitive state, they must be repeated multiple times in order to be independent of potential external factors or events unrelated to the participant's cognitive state, such as misunderstanding how to complete the task or equipment malfunction.

Another flaw is that the exercises were not randomized, that is to say, all pre-experimental tasks were the same for every participant, and every post-experimental task was also the same for every participant. The issue with this is that some individuals participated in both the train and the music experiments. This means that they had already done the exact same tasks with the exact same answers before. The repetition effect therefore makes the results less reliable

To remove these flaws, we decided to create a new and improved version of the same tool. Our new construct is designed to generate more robust and reliable results, to be easy to use and tailored to different users, more precisely to distinguish between users with pre-clinical AD and AD This chapter explores the particularities and design of such a tool.

5.4.2. Tool Description

This tool was developed using the Unity 2D game engine. It consists of an environment with randomized cognitive exercises tailored to the participants suffering from either SCD or AD. A new addition to this tool is its ability to display improvement measurement results using graphics which are easy to read. This enables users to easily see their cognitive performance after the intervention with reference to their performance prior to the intervention. Furthermore, cognitive readings can be saved into the user's system account, enabling caretakers to easily track the user's cognitive functions through time.

Just like its predecessor, this tool is made to be used in conjunction with an intervention, as can be seen in the tool experimental procedure shown in figure 26.

5.4.2.1 Tool Experimental Procedure

To make use of this tool, participants must first be classified as either suffering from SCD or AD. According to their classification, the tool will change the set of exercises in order to be suitable for the participant. Participants classified in the SCD group will have a series of 4 exercises to complete, whereas the AD group will have to perform 6 exercises (see Table III).

Once the participant has completed the cognitive exercises, they are immersed in a virtual therapeutic environment. After the intervention, the participant completes once again different variations of the same randomized cognitive exercises. Based on the pre- and post-intervention performance, the tool will display graphical information about the participant's cognitive state progression.

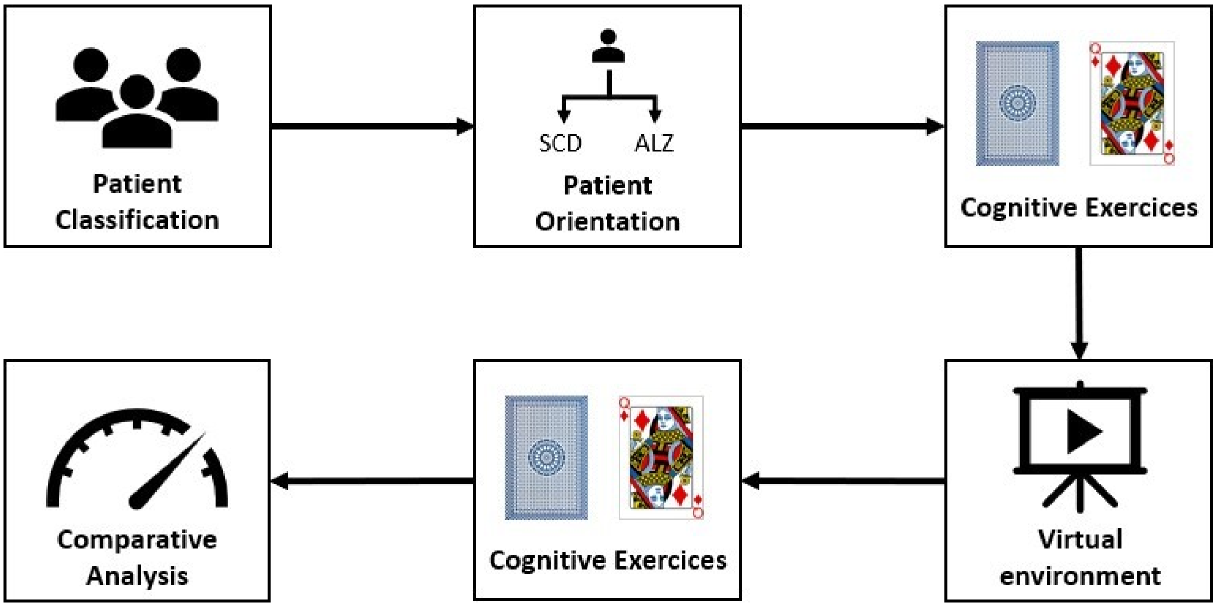

Figure 26. Performance tool architecture. SCD, subjective cognitive decline; ALZ, Alzheimer's disease.

5.4.2.2 Exercises

The exercises are based on the CogState exam [77], which have repeatedly been shown to be accurate. They are made to have little to no practice effect, therefore the participant can perform the same exercises, multiple times, and not obtain a better performance due to repetition and practice. Below are descriptions of the exercises used for this tool. Table III shows which ones are used for SCD and for AD participants.

One Back Test: In this task, the card on screen is continuously being flipped after a short delay, revealing a new card. Participants must say if the current card is the same as the previous one. This exercise tests working memory and is presented in figure 27. In this example, participants must answer *same* (*pareille*) if the previous card was a jack of hearts, or *different* (*pas pareille*) otherwise.

Figure 27. One back test screen capture.

One Card Learning Test: In this task, the card on screen is continuously being flipped after a short delay, revealing a new card. Participants must say if they have or have not seen this card before. This exercise tests visual learning and is presented in figure 28. In this example, participants must answer *have seen* (*déjà vue*) if they have already seen this card, or *have not seen* (*jamais vue*) otherwise.

Figure 28. One card learning test screen capture.

Detection Test: In this task, the card on screen is continuously being flipped after a short, varying delay. Participants must say when the card has flipped as quickly as possible. This task measures the participant's reaction time and tests psychomotor function (see figure 29).

Figure 29. Detection test screen capture.

Identification test: In this task, the card on screen is continuously being flipped after a short delay, revealing a new card. Participants must identify if the card is black or red. This exercise tests attention and is presented in figure 30. In this example, the correct answer would be *black* (*noir*).

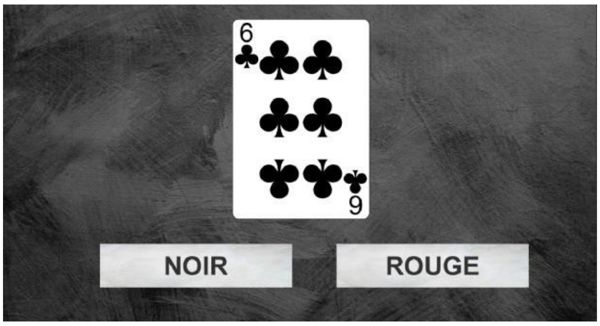

Figure 30. Identification test screen capture.

International Shopping List Test: In this task, participants must observe as four words appear one after the other on screen. After a delay, a list of words is presented to the participant, and the participant must select the words what were previously shown on screen. This exercise tests verbal learning and is presented in figure 31. In this example, one of the four correct answers would be *Pizza*.

Figure 31. International shopping list test screen capture.

Continuous Paired Associate Learning Test: In this task, cards are scattered across the screen and the participant must flip them, two at a time, and find the matching pairs. The cards have abstract drawings on them. This exercise tests paired associate learning and is presented in figure 32. In this example, the participant has found one of the four matching pairs.

Figure 32. Continuous paired associate learning test.

As previously mentioned, this tool offers two different modes according to the participant's characterization. The following table shows the exercises used for the performance evaluation of pre-clinical AD and AD participants.

Table III. Exercises for the different participant options of the tool. Exercise descriptions are provided in the text.

Exercises	Pre-clinical AD	AD
One Back Test: *Working memory*	✓	✓
One Card Learning Test: *Visual learning*	✓	✓
Detection Test: *Paired Associate Learning*	✓	✓
Identification Test: *Attention*	✓	✓
International Shopping List Test: *Verbal learning*		✓
Continuous Paired Associate Learning Test: *Paired Associate Learning*		✓

5.4.3. Experiments

Due to the Covid-19 pandemic, experiments could not be performed with this tool. Some features of the tool are still underway and will be finished shortly. Future lab projects will be able to use and test the tool.

Chapter 6. Conclusions and Future Works

This thesis explored the therapeutic potential of virtual reality (VR) in interventions targeting people with subjective cognitive decline. More precisely, we aimed to verify the following:

1. Is it possible to reduce negative emotions and increase positive emotions through virtual environments?
2. Do our virtual environments improve cognitive functions which are often early symptoms of Alzheimer's disease (AD)?

With this in mind, we created and tested two virtual environments: travel therapy by virtual train, and music therapy in a virtual theatre. Results showed that affective states were generally improved following the immersive experience. These results were based on the analysis of frustration and valence through the progression of the experimental session. On a cognitive level, performances on attention and memory exercises were generally improved. The most notable result was the mean performance improvement on the last memory exercise for the music therapy environment, which reached a general mean performance increase of roughly 37%.

The second part of this thesis aimed to create a cognitive performance measurement tool specifically designed for individuals with pre-clinical AD, and diagnosed AD. To this end, we created a tool containing a variety of cognitive tasks targeting specific brain functions. Based on the answers provided by the participant prior to and following an intervention, the tool displays the cognitive function improvements, tracking if there are increases or decreases in specific executive functions. This tool was not tested due to the Covid-19 pandemic.

Our results proved our environments' efficacy in improving affective and cognitive states. Given these encouraging results, our research group is developing new virtual environments with the same objectives. The goal is to create a hub of different environments from which either an intelligent agent or a user could select from. In making the virtual environment hub easy to use, we believe that this novel approach to treating symptoms of AD could be very beneficial in the context of elderly centers. Indeed, this would enable older users to manipulate the technology more easily, making them independent of staff and caretakers in that regard.

Furthermore, we believe that once enough experiments have concluded the efficacy of the virtual environments, it could be possible and even advantageous to remove the EEG headset from the treatments. Since the EEG headset's primary purpose was to obtain confirmation and measurements of the virtual environment's effects on participants, it's use will no longer be necessary for environments with tested and confirmed efficacy results. While the music environment is based on the participant's emotional response and thus makes use of the EEG recordings, we argue that perhaps eye movement analysis using an eye-tracking device and techniques could replace the EEG recordings. The removal of the EEG headset could be a game changer, as the installation of the equipment would be reduced to only putting on the VR headset. This would mean that individuals would not have to rely on staff members to properly install the EEG electrodes and would make the experiment that much easier. Users could autonomously use this technology.

On a more specific level, future works on the music therapy environment could explore the integration of a wider selection of songs tailored to the participant. More than one experimental session would be required in order to identify the participants' preferences, or meetings with the family could help create a suitable playlist. Progressively, the environment would tailor itself to each participant in a way that very well may increase the environment's positive effect on affective state and cognition. Moreover, future projects could explore the cognitive performance measurement tool's potential for conditions other than pre-clinical AD and diagnosed AD. More exercises could be added to the tool, enabling to create different modes for various neurological conditions, such as depression anxiety disorders, brain injuries and perhaps even epilepsy.

Since this technology's administration is not conditional to, for example, the absence of certain medications or to certain physical abilities, as is the case for some pharmacological treatments, we believe that this method would be widely accepted from individuals suffering from AD, or even a wider population.

With the rapid and constant evolution of technology and machine-learning, we can envisage that these therapeutic environments could evolve alongside them. Indeed, improvements such as less cumbersome headsets, the use of different biometrics for analyses (i.e. eye-tracking) and new machine-learning techniques could make these environments even more powerful. For example, the integration of reinforcement learning in our therapeutic environments could provide tailored environmental adaptations for each participant and consequently improve the efficacy of the treatments. The integration of VR in therapeutic contexts is full of potential, and we are only just at the beginning.

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Appendix A: Conference Article 1

Published Paper in 9th International Conference on Sensor Networks, 2020:

Application of Virtual Travel for Alzheimer's Disease

Conference

Sensor Networks, 9th International Conference, SENSORNETS 2020, Valletta, Malta, February 28-29, 2020

Author Contribution

Researchers at the Université de Montréal

Hamdi Ben Abdessalem: Development of virtual environment. Integration and testing of the product. Development of cognitive exercises. Performing experiments with Participants in France. Results analysis.

Claude Frasson: Development of idea to a feasible product. Supporting, funding and reviewing the project.

Alexie Byrns: Original idea of virtual environment.

Researchers at Institut de Gériatrie de l'Université de Montréal

Marc Cuesta: Reviewing paper.

Marie-Andrée Bruneau: Reviewing paper.

Sylvie Belleville: Reviewing paper.

Researchers at the Université Côte d'Azur

Valeria Manera: Performing experiments in France. Reviewing work.

Philippe Robert: Performing experiments in France. Reviewing work.

Application of Virtual Travel for Alzheimer's Disease

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Keywords: Healthcare Applications, Sensor Networks Applications, Virtual Travel, Cognitive Environments, Alzheimer's Disease, Immersive Environments, Emotions, EEG Sensors.

Abstract: Negative emotions such as anxiety, frustration, or apathy can have an impact on the brain capability in terms of memory and cognitive functions. This is particularly visible in Alzheimer's disease where the participants can have a deterioration of their brain connections which are often the cause of the disorders detected in Alzheimer's participants. It seems important to reduce these symptoms to allow better access to memory and cognitive abilities. Immersion in Virtual Reality is a means of providing the participant with a sense of presence in an environment that isolates them from external factors that can induce negative emotions. The virtual travel is a method that can mobilize the attention of the subject and revive their interest and curiosity. We present here, an experiment in which a participant is immersed in a virtual train using a virtual headset and EEG device to measure the brain signals. To measure the impact of this train on the memory and cognitive functions, some cognitive tasks have been included before and after the travel. Experiments have been done on participants with mild cognitive disorder. Preliminary results show an increase of memory functions and in certain cases of cognitive functions, while negative emotions are reduced.

1 INTRODUCTION

Emotions and motivation play an important role in cognitive tasks. It is well known that stress or anxiety during a test can make students forget key components of the answers or solutions to the problems they must find. In fact, negative emotions such as anxiety, frustration, or lack of interest such as apathy (Robert et al., 2018; Zhu et al., 2019) have an impact on the brain capability in terms of memory and cognitive functions. This is particularly visible in older adults with Alzheimer's disease (AD) and related disorders as individuals have reduced brain reserve which may make them particularly vulnerable to the effect of negative emotions.

AD is the most common form of dementia and with the aging population, prevalence increases dramatically. It is estimated that by 2050, 11 to 16 million persons will be diagnosed with AD in the U.S. alone (Association, 2015). Despite intensive research, effective pharmacological treatment has yet to be discovered. Focus has therefore started to shift towards non-pharmacological approaches to reduce the impact of symptoms on autonomy and well-being.

Virtual reality (VR) has proven to be efficient in treating certain disorders, such as phobia (crowd, elevators, spiders) and can be used to reduce negative emotions. The world in which a user is immersed provides a feeling of safety and encourages imagination. Also, the user is isolated from external factors which can induce negative emotions. In this scope, we have created a virtual train in which participants are immersed and travel virtually looking through the windows to the landscape. A major difference between our approach and the existing ones which use projection on a screen is that the participant is equipped with a virtual headset and can freely navigate in the train, turning their head and looking around as if they were in a real train. Another major innovation of our work is that we measured emotions with an electroencephalography (EEG) device, coupled with eye tracking techniques to detect what the subject is looking at. Techniques such as EEG and eye tracking, have been up to recent years

(Ben Khedher et al., 2018; Berka et al., 2007; Maynard et al., 2013; Ben Abdessalem et al., 2019) mainly used in strict laboratory conditions, but are increasingly used in realistic emotional and learning settings (Ben Khedher et al., 2019). Their capacity to offer real-time qualitatively rich information about the users' state has tremendous potential to assess emotions coupled with VR immersion.

We conducted experiments with participants in older adults with subjective cognitive decline in order to verify the following hypotheses; **H1**: **is it possible to reduce negative emotions of the participant through virtual travel?** And **H2**: **Does this system improve memory and cognitive functions?**

The rest of this paper is organized as follows. In Section 2, we give an overview of the characteristics of AD. In Section 3 we provide an overview of virtual immersive environment and our solution with the virtual train. In Section 4, we detail the experimental procedure, the cognitive tests and the physiological sensors that we use, and finally, in Section 5 we present and discuss the obtained results.

2 CHARACTERISTICS OF ALZHEIMER'S DISEASE

2.1 Origin of Alzheimer's Disease

Alzheimer's disease (AD) is a neurodegenerative disease which progressively gets worse over time. Its most notable symptom is the deterioration of both short- and long-term memory. The disease also affects behavior, cognitive abilities as well as physical abilities in affected individuals. Much research has been conducted, investigating the causes and underlying mechanisms of AD. These revealed the significant role of neural damage in specific regions of the brain. With the accumulation of this damage, the disease ultimately interferes with the individual's capacity to perform activities of daily living, rendering them dependent of caregivers (Association, 2015).

The progressive decay characteristic to AD is suggested to be a result of the gradual loss of structure and neural function. The affected regions in large part involve the cortex, the limbic system and the hippocampus (Association, 2015). These regions play major roles in memory, emotions and higher-order functions such as attention and thought. It is proposed that symptoms of apathy could help identify individuals at higher risk of the disease (Dubois et al., 2007; van Dalen et al., 2018). As the disease progresses, patients begin to display impaired cognitive and functional abilities, resulting in difficulties in decision-making, daily tasks, communication and memory retrieval. Individuals also experience a decrease in general interest and often become apathetic. During the final stages of the disease, patients become practically incapable of communicating, have difficulty eating and display extreme apathy (Association, 2015).

AD is also characterized by important atrophy in distinct regions of the brain. Among the first structures to suffer brain damage is the hippocampus, which displays significant neuronal death. With the hippocampus being a key structure in memory, its damage is directly linked to memory loss in AD. The cortex, which is responsible for higher-order functions such as attention, awareness, thought and memory, also experiences important atrophy (Pini et al., 2016).

2.2 The Effect of AD on Non-cognitive Symptoms and Quality of Life

With time, AD patients become increasingly reliant of their caregivers and progressively unaware of their condition. Studies focusing on quality of life of patients investigated the difference between the caregivers' perception of the patient's appreciation of life and patient's own appreciation. The study revealed that caregivers perceive the patient's quality of life as significantly worse than the patient's own perception (Zucchella et al., 2015).

Another study investigated the frequency of positive and negative emotions in both AD and non-AD patients. The results showed that AD patients experienced significantly more negative emotions than non-AD patients (Lawton et al., 1996). With apathy, confusion and loss of self being marked symptoms of AD, it is possible that subjective reports of quality of life from patients tend towards more neutral levels of appreciation since individuals lose reference to themselves and can poorly evaluate their own state.

2.3 Virtual Reality as an Intervention for Alzheimer's Disease

There have been many reports revealing benefits in using VR with AD patients. The dynamic, multisensory and interactive aspect of VR allows for a strong ecological validity (Cherniack, 2011). There is some indication that VR intervention with computerized cognitive training can improve cognitive domains in individuals with mild cognitive impairment or AD (Coyle et al., 2015; Hill et al., 2016). Moreover, participants prefer completing cognitive training tasks in VR over its pencil-paper counterpart (Manera et al., 2016). It is proposed that more engaging training will be more effective.

As of now, most studies focus on how VR can help participants at the cognitive or psychological level (Appel, 2017; Biamonti et al., 2014; Laforte, 2018). However, a growing body of research is now investigating the power of VR at a more physiological level (Todd & Anderson, 2009; Vindenes et al., 2018). For instance, immersion in a virtual environment may alter synaptic activity in such a way as to affect interstitial βA levels (Cirrito et al., 2005) leading to tangible behavioral and cognitive benefits.

3 VIRTUAL IMMERSIVE ENVIRONMENTS

3.1 Virtual Reality

Over the last few years, VR started to be used in many fields due to its remarkable advantages, the major one being full immersion. In fact, VR tricks the mind of the users and increases their sense of presence in the virtual environment. It makes them believe that they are in a real world and promotes performance (Biocca, 2006). Therefore, VR is increasingly being seen as the most interesting way to present an environment to users.

The main advantage of virtual reality compared to other interactive environments is that the user is isolated from external visual distractions. This technology has been applied in the field of psychology to treat various disorders, including brain damage (Rose et al., 2005), anxiety disorders (Gorini et al., 2008) and alleviation of fear (Alvarez et al., 2007). For instance, Pedraza-Hueso et al. (Pedraza-Hueso et al, 2015) introduced a VR system which consists of different types of exercises with which the user can train and rehabilitate several aspects including cognitive capacities.

3.2 The Therapeutic Train: Our Inspiration

A study published in 2014 (Biamonti et al., 2014) investigated the impact of a virtual train travel on people with AD. Installations recreating a fictitious train station were placed in the retirement home to simulate a real train station. Older adults participating in the study were encouraged to take a train ticket at the fake ticket office, and to wait for the train to arrive in order to maximize the realism of the trip. The trips lasted a maximum of 30 minutes and ended when the train arrived at the next fictional station.

In this study, the researchers tested two different types of virtual trains: the first prototype consisted of two wooden doors that opened and led to a room with two armchairs, a small table and a lamp. To simulate the "train windows", there were two LCD screens that showed videos taken by a real train. A total of 20 individuals tested this prototype. The second prototype was more complex, created in collaboration with the research group, an architect and therapists. The appearance of the train was much more realistic, and the car was isolated from the rest of the retirement home, which was not the case for the first prototype. A total of 37 individuals tried this prototype.

For the first prototype, no positive results were obtained but the second prototype was more efficient. With its more realistic look, 31 of the 37 participants who tested the second prototype admitted to being in a train, while this was the case for none of the participants who had tried the first prototype. The results show that the train reduced wandering (in 9 of the 12 participants with wandering), reduced agitation (in 8 of the 9 participants with agitation), and positively influenced anxiety, apathy and sleep (Biamonti et al., 2014).

3.3 The Virtual Train

The previous environment was not a virtual environment but a simulation of a real train station. As indicated in the section above, a virtual environment could be a great solution to improve the mood of AD people. The principle of immersion is crucial for isolating the subject from the real world, providing a relaxing environment and reducing negative emotions (which on the other hand can still be present in a simulated environment such as Biamonti’s work). So, in order to achieve our first goal which is reduce negative emotions of the participant through virtual travel, we started by designing and creating an immersive virtual travel environment. To this end, we used Unity3D game engine which contains a built-in physics engine able to simulate real aspects of our virtual travel. This environment represents a virtual train in which the participants find a happy family sitting next to them (Figure 1). The virtual train goes through 3 different environments. The first one is about a forest with trees and pacific animals.

Figure 1: Screen capture of the virtual train.

In the second one, the train goes through a snow environment with mountains and pacific animals (Figure 2). The third and last environment is about a sunny desert with a warm sun.

Figure 2: Screen capture of the virtual train (second environment).

4 EXPERIMENTS

In order to analyze the impact of the virtual train on the memory and cognitive performances (particularly attention), we created 6 attention and memory exercises.

Attention exercises: In the first exercise, the participant hears a series of numbers and is asked to repeat them in the order of presentation using a numerical pad; they are then presented with another series of numbers but are now asked to report the numbers in the backward order. Figure 3 shows how the participant can interact with this exercise through the numerical pad.

The second test is a selective attention exercise in which the participant hears a list of letters at a rate of one item per second and is asked to click the space bar every time they hear the letter “A”.

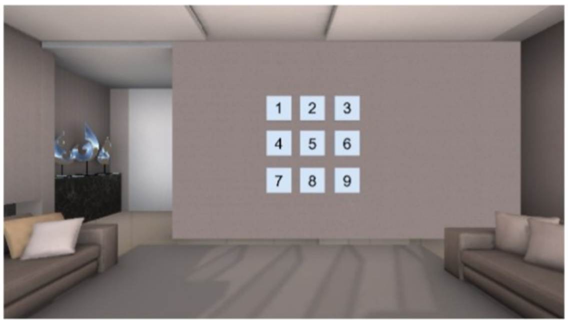

Figure 3: Screen capture of exercise 1.

In the third exercise, we show images of different objects for a short period of time. The image is then replaced by a series of four letters and the participant is asked to select the first letter of the object that was just presented. Figure 4 and 5 show a screenshot of the third exercise.

Figure 4: Screen capture of exercise 3.

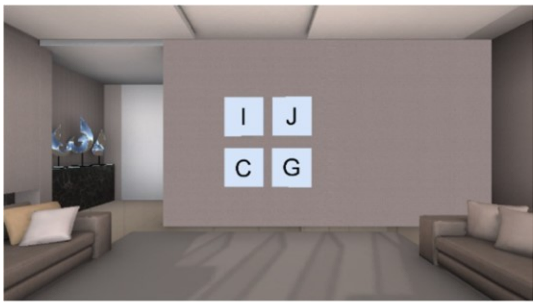

Figure 5: Screen capture of exercise 3.

Memory exercises: For the first exercise, participants are asked to memorize a series of objects presented visually or orally with their name. Participants are then presented to a series of object images or words presented auditorily. Participants are asked to determine whether the object was seen visually, auditorily or never presented if the object was not present. For instance, Figure 6 shows an image of an airplane, and the participant should select if they saw it, heard its name, or if the object was not present in the previous sequence. In Figure 6, the participant already saw the picture of the plane, so they select "Deja vu" (already seen in French).

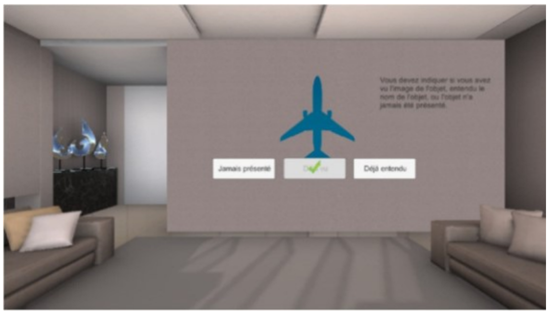

Figure 6: Screen capture of exercise 4.

In the fifth exercise, several circles are presented to the participant. A series of these circles is highlighted one by one in order to create a sequence. The participant is asked to memorize and reproduce the same sequence. Figure 7 shows a screenshot of the circles while one is highlighted.

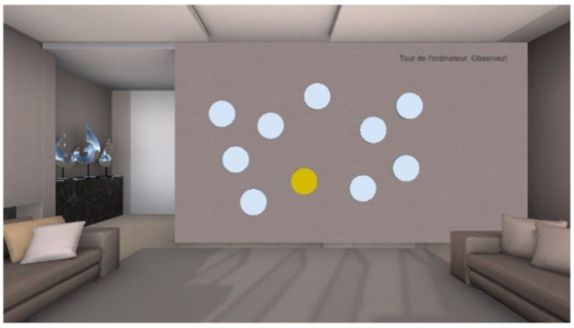

Figure 7: Screen capture of exercise 5.

In the sixth and final exercise, participants are asked to memorize sets of three pictures for a short period of time. Then, we present four sets of three pictures and the participant is asked to select the set which corresponds to the one they saw. Figure 8 and 9 show an example of this exercise.

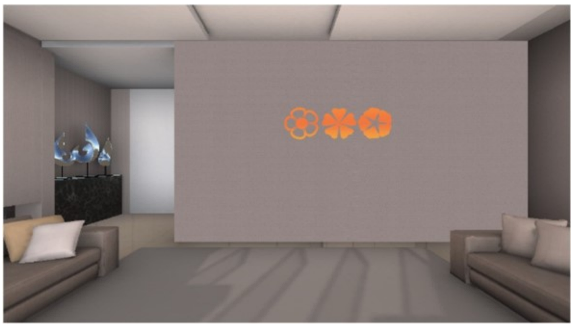

Figure 8: Exercise 6: Set to be memorized.

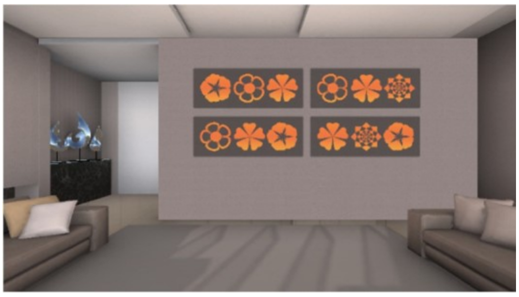

Figure 9: Exercise 6: Four sets from which the correct set should be identified.

We tested our approach in 19 participants (11 Females) with subjective cognitive decline (SCD) and a mean age = 69.68 (SD= 5.49). The participants took part in two sessions. In the first one, they attended a pre-experiment session (one hour) in which we made sure that they met eligibility criteria to make the experiment. Our eligibility criteria were the following:

- Older than aged 60 of age
- Francophone
- Normal or correct-to-normal vision
- Normal hearing
- Met the Consortium for the Early Identification of Alzheimer's Disease – Quebec (CIMA-Q) criteria for SCD:
    - Presence of a complaint defined as a positive answer to the following statements: "my memory is not as good as it used to be" "and it worries me"
    - MoCA 20-30
    - No impairment on the logical memory scale based on the education-adjusted CIMA-Q cut-off scores.

During the pre-experimental session, participants were provided with oral and written description of the study and invited to sign a consent form. The session then included the clinical tests that are necessary to confirm diagnosis and characterize participants. If the participants were eligible, they were invited to the experiment which took place within the following 15 days.

In the experimental session, the participant was first invited to fill the Positive and Negative Affect Schedule (PANAS) scale (Watson et al., 1988) a self-assessment of emotions, and the questionnaire of cyber-sickness (Kennedy et al., 1993). We then equipped participants with an EEG headset. When the exercises were completed, we equipped them with the Fove VR headset, and they started the immersive virtual train experience. The virtual travel lasted about 5 minutes. Following the virtual travel, participants completed the cognitive and memory tests again (using different examples). And they filled-up the PANAS scale, cyber-sickness, AttrakDiff 2 (Lallemand et al., 2015), and a self-report form. The AttrakDiff 2 scale allows to evaluate the user experience through 28 items on attractiveness, pragmatic quality and hedonic qualities (stimulation and identity) of the virtual environment. Figure 10 shows the different steps of the process of the experiment.

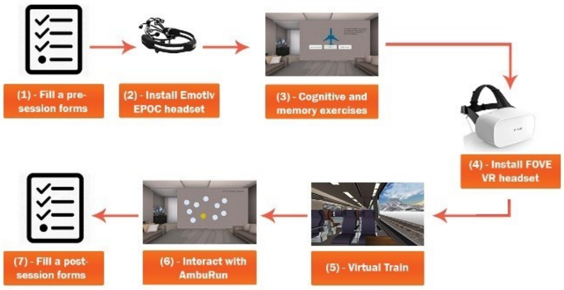

Figure 10: Process of the experiment.

4.1 EEG Measures

In this study, we used Emotiv Epoc+ EEG headset technology to track the excitement of the player. The headset contains 14 electrodes spatially organized according to International 10-20 system, moist with a saline solution. The electrodes are placed at antero-frontal (AF3, AF4, F3, F4, F7, F8), fronto-central (FC5, FC6), parietal (P7, P8), temporal (T7, T8) and occipital (O1, O2) regions with two additional reference sensors placed behind the ears. The detailed position of the measured regions is shown in Figure 11.

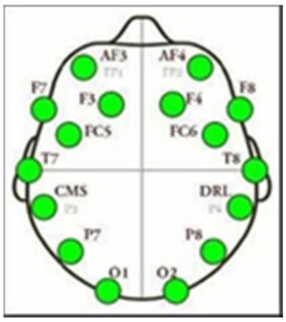

Figure 11: Emotiv headset sensors placement.

Emotiv system generates raw EEG data (in µV) with a 128Hz sampling rate as well as the five well-known frequency bands, namely Theta (4 to 8 Hz) Alpha (8 to 12Hz), low Beta (12 to 16 Hz), high Beta (16 to 25 Hz) and Gamma (25 to 45 Hz). Furthermore, the system uses internal algorithms to measure the following mental states: mediation, frustration, engagement, excitement and valence. They were used to assess the effect of the virtual train on the emotions of participants.

Even though we don't have access to the system proprietary algorithms to infer these mental states from the raw data and the frequency bands, several studies have established the reliability of the output (Aspinall et al., 2015).

5 RESULT AND DISCUSSION

The first objective of this research was to discover whether it is possible to reduce negative emotions of the participant through a virtual travel. To this end, we started by analyzing the emotions of the participants before, during and after the virtual train immersion. The results show that the mean frustration of participants before the therapeutic train was *0.71*, (minimum *0.41* and maximum *0.96)*. The participants' mean frustration during the travel in the train was *0.51* (minimum *0.24* and maximum *0.94)*. After the therapeutic train, the mean frustration was *0.53* (minimum *0.17* and maximum *0.79)*. Figure 12 shows a boxplot of the mean frustration before, during and after the travel in the virtual train.

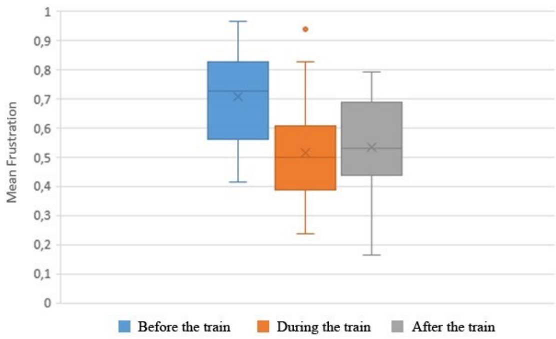

Figure 12: Boxplot of general mean frustration.

Thus, the frustration decreased when the participants were in the virtual train and the positive effect on frustration was still observed after the virtual train. Furthermore, in individuals whose frustration increased after the train immersion, their frustration level never reached its prior level.

Individual results are shown in Figure 13, in which we note that the frustration decrease that was found when considering the group mean is observed in 17 of the 19 participants. Only participant 9 and 12 failed to show the effect.

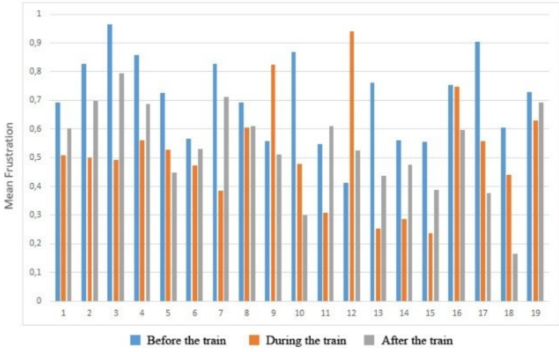

Figure 13: Histogram of mean frustration in individual participants.

An effect on frustration is also observed when examining participants' self-report. Before the train, 31,6% of them reported that they were stressed. After the train, only 15,8% of them reported that they were stressed.

The effect obtained in our first analysis lead to our second research question which is: does this system improve cognitive (attention) and memory functions? To this end, we analyzed performance improvement on the three attention exercises. On exercise 1, the general mean improvement was negative by 6.58%. On the second exercise, there was a mean improvement of 0.48%. The performance improvement on the third exercise was 7.02%.

More detailed results are shown in Figure 14. When comparing performance for exercise 1 prior to and after the virtual train, four participants showed improvement, seven decreased performance and eight participants kept the same performance. Only one participant showed improvement on exercise 2, while the others kept the same performance. Finally, on the third exercise, 4 participants showed improvements and the others kept the same level of performance.

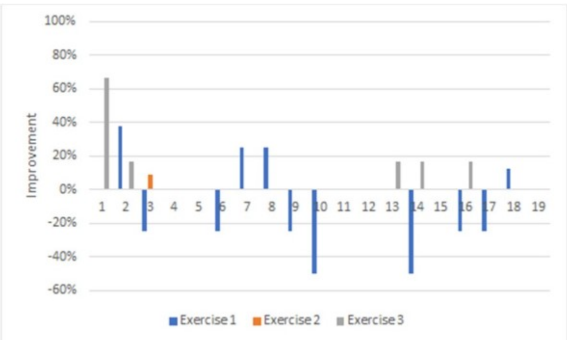

Figure 14: Histogram of performance improvement in exercise 1, 2 and 3.

We also analyzed the performance improvement for the three memory exercises. For exercise four, a 10.53% mean improvement is observed. For the fifth exercise, the mean improvement is 20% which is the highest percentage of improvement. Finally, the mean improvement is 10,53% for exercise six.

Individual results are shown in Figure 15, in which we can see that for the fourth exercise, nine participants had improvement, two participants had a decrease of performance, and the rest kept the same level of performance. For exercise 5, eleven participants showed improved performance while one kept the same level of performance and the eight had a decrease of performance. Finally, five participants improved on the last exercise, while four of them had a decrease of performance and the rest kept the same level of performance. We note that it is in this exercise that a participant showed the highest improvement performance with participant 1 showing a 100% improvement. Finally, participant 6 was unable to perform the exercise before the train and succeeded after the train.

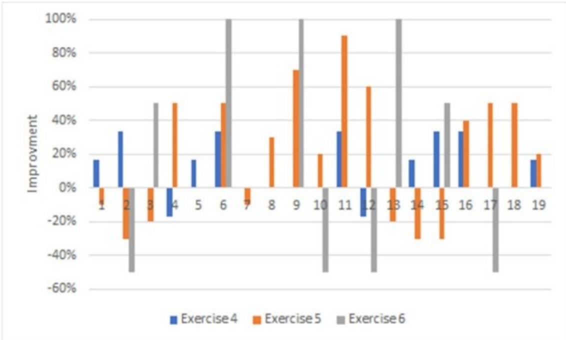

Figure 15: Histogram of performance improvement in exercise 4, 5 and 6.

Finally, we compared improvement in cognitive exercises versus memory exercises. To this end, we grouped the exercises into two groups, and we calculated by averaging the mean performance improvement for exercises 1, 2 and 3 (cognitive/attention) and 4, 5 and 6 (memory). Figure 16 shows a clear difference between the improvement of performance on the cognitive exercises versus the memory exercises.

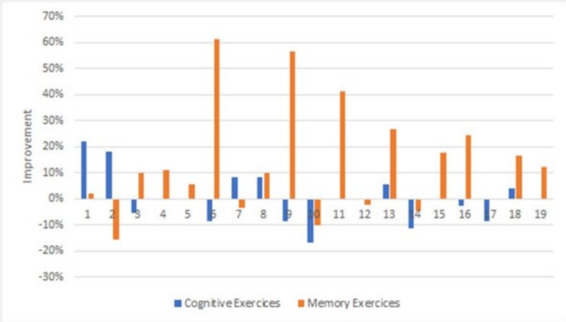

Figure 16: Histogram of performance improvement cognitive vs memory exercises.

These results show a clear increase in memory performance following the virtual train and in some cases an improvement in attention abilities. Negative emotions like frustration, are reduced. A post-experience evaluation questionnaire confirmed that the virtual train is relaxing and reduces stress (73,7% participant confirmed that the virtual train is very relaxing). The questionnaire confirmed the participants' interest for this method, and their appreciation of virtual reality and its immersion effect. In fact, 89,5% of them confirmed the good aspect of immersion and 79% confirmed also that VR has a positive impact on their experience.

6 CONCLUSION

In this paper, we presented a novel approach which could be used to improve AD patients' memory performance using a virtual train. Experiments were conducted during which the participants performed cognitive and memory exercises, then travelled in the virtual train in order to relax them, and then performed the memory and cognitive exercises again. Results showed that the virtual train helps relax the participants and decreases negative emotions, most notably frustration. In addition, results showed that the participants' performance in the attention exercises did not improve or improved very mildly. On the other hand, the participants' performance on the memory exercises was improved.

The first hypothesis (reducing the negative emotions) was clearly reached. The second hypothesis was partly accomplished. We can improve the memory performance of the participants by using the immersive virtual train which is a consequence of reducing the negative emotions.

These results indicate that the virtual train can reduce negative emotions and that this might have a positive impact on the memory performance of older adults.

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Appendix B: Conference Article 2

Published Paper in the 16th International Conference on Intelligent Systems, 2020:

Adaptive Music Therapy for Alzheimer's Disease Using Virtual Reality

Conference

Intelligent Tutoring Systems, 16th International Conference, ITS 2020, Athens, Greece, June 8-12, 2020

Author Contributions

Researchers at Université de Montréal

Hamdi Ben Abdessalem: Integration and testing of the virtual environment. Development of cognitive exercises. Performing experiments with participants at IUGM. Results
analysis.

Claude Frasson: Development of idea to a feasible product. Supporting, funding and reviewing the research.

Alexie Byrns: Development of the virtual environment.

Researchers at the Institut de Gériatrie de l'Université de Montréal

Marc Cuesta: Performing experiments at IUGM. Reviewing paper.

Marie-Andrée Bruneau: Performing experiments at IUGM. Reviewing paper.

Sylvie Belleville: Performing experiments at IUGM. Reviewing paper.

Adaptive Music Therapy for Alzheimer's Disease Using Virtual Reality

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Abstract. With Alzheimer's disease becoming more prevalent, finding effective treatment is imperative. While no pharmacological treatment has yet proven to be efficient, we explore how technology can be integrated into non-pharmacological intervention to enhance its benefits. We propose a new and unique version of Music Therapy, an already existing therapy known to be beneficial. Music therapy has been shown to improve emotions and certain cognitive functions, which is the main focus of our study. To this aim, we designed a virtual reality environment consisting of a music theatre in which participants are immersed among the audience. A meticulously chosen selection of songs is presented on stage accompanied by visual effects. Results show that the environment decreases negative emotions, increases positive emotions, and improved memory performances were observed in most participants following the immersive experience. We speculate that by improving emotions through adaptive music therapy, our environment facilitates memory recall. With virtual reality now being easily accessible and inexpensive, we believe this novel approach could help patients through the disease.

Keywords: Virtual reality · Alzheimer's disease · Music therapy · EEG · Intelligent health application · Emotions

1 Introduction

Alzheimer's disease (AD), the most common form of dementia, is rapidly becoming more prevalent as the population ages. By bringing about progressive cognitive impairment and neuropsychiatric symptoms, AD causes discomfort and suffering for both patients and caregivers. As no pharmacological treatment has yet been discovered, research has started to shift towards non-pharmacological interventions. Recent technological advances have made it easier to design non-pharmacological approaches aimed at increasing patient well-being. We believe introducing Virtual Reality (VR) in this new field of study is a promising avenue.

Indeed, VR has proven to be useful in a variety of therapeutic interventions, such as anxiety disorders and phobias [1]. Most VR environments are however unable to

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evolve according to the reactions of the patient. An important characteristic of AD is that it is accompanied by negative emotions, which may have an influence on cognitive abilities and memory access [2]. Empirical and anecdotal reports have pointed towards an already-existing non-pharmacological intervention, Music Therapy (MT), as a promising avenue in helping AD patients on a psychological, behavioral and cognitive level [3, 4]. For this reason, we designed a virtual environment which combines the benefits of both VR and MT, potentially giving rise to an accessible and low-cost solution to personalized MT. To adapt the environment to the patient, our design uses a measure of the participant's emotions to make parameters of the environment adapt to the measured emotions. We focus our research on older adults with subjective cognitive decline (SCD), as these individuals progress to dementia at a higher rate than those with no subjective impression of decline and are sometimes in the early stages of the disease [5].

With these design objectives, our research questions are the following: Q1: is it possible to reduce negative emotions through virtual music therapy? And Q2: is it possible to improve memory and cognitive functions through adaptive virtual music therapy?

The rest of this paper is organized as follows. In Sect. 2, we give an overview of the characteristics of AD. In Sect. 3, we examine how music can provide a therapy for Alzheimer's disease and we present our solution of adaptive virtual reality environment. In Sect. 4, we detail the experimental procedure undertaken to validate our hypotheses. Finally, in Sect. 5 we present and discuss the obtained results.

2 Characteristics of Alzheimer's Disease

Alzheimer's disease (AD) is a neurodegenerative disease whose most notable symptom is the deterioration of both short- and long-term memory. In addition to memory impairment, the disease affects behavior, non-memory cognitive abilities and physical abilities. Much research has revealed that neural damage in specific regions of the brain plays a significant role in the symptoms of AD [6].

As patients progress in the disease, cognitive and functional abilities become significantly impaired, resulting in difficulties in decision-making, daily tasks and communication. Individuals also experience a decrease in general interest and often become apathetic. During the final stages of the disease, patients become practically incapable of communicating, have difficulty eating and display extreme apathy [7].

3 A Music Therapy Virtual Environment with Adaptation for Alzheimer's Disease

3.1 Music Therapy

Music displays great therapeutic potential for many neuropsychiatric conditions and AD is no exception. Indeed, empirical evidence suggests that music therapy (MT) can help improve cognitive, psychological and behavioral impairments induced by the disease [3, 8].

There are already many studies showing the benefits of MT for AD patients [3, 4, 8]. We propose to combine MT with a VR environment and an electroencephalogram device (EEG) able to assess the emotions felt by the participants. By focusing on the underlying neurological mechanisms which give music its therapeutic capability, we designed a new version of MT. As AD patients struggle at an emotional, cognitive, psychological and behavioral level, we target these symptoms directly.

3.2 Adaptive Virtual Reality Music Environment

Our therapeutic environment consists of a music theatre created using Unity 3D software in which the participant is immersed, facing the stage up front. Red curtains open and close as different songs are presented on stage. For each song, an appropriate selection of instruments is presented on stage, each instrument slightly animated with the music. In addition, the stage presents firework-like light visual effects taken from the Unity 3D Asset Store. These are designed to fit each individual song (Fig. 1).

Fig. 1. The virtual MT environment for two different songs.

The choice of music was based on empirical studies and theories of music [9–11]. A series of eight 30 s song excerpts are sequentially presented, accompanied by visual scenes designed with specific color shades and lightings in order to achieve the emotional purpose of the song (relaxation, engagement, etc.) [12].

In order to optimize the emotional and cognitive impact of the virtual experience, the environment was adapted to provide the most beneficial therapeutic experience to each individual participant.

4 Experiments

In order to analyze the impact of the Music Therapy environment on memory and attention performances, we created 6 attention and memory exercises using Unity 3D software.

Our approach was tested on 19 participants (13 females, 6 males) with subjective cognitive decline (SCD) and a mean age = 72.26 (SD = 5.82). The participants took part in two sessions: the first one to ensure eligibility for the study and the second one for the actual experiment. During the pre-experimental session, participants were invited to sign a consent form and perform clinical tests to confirm diagnosis of SCD and characterize them.

The second session was the experimental session. Participants were first invited to fill questionnaires: the Positive and Negative Affect Schedule (PANAS) scale [13], a self-assessment of emotions, and a questionnaire on cyber-sickness [14]. Once completed, the participants were equipped with an EEG headset and asked to solve attention and memory exercises. Following the cognitive tests, a FOVE VR headset was installed and the VR MT began. This relaxing environment lasted for about 10 min. Following the MT, participants completed again different variants of the same attention and memory tests. Lastly, the participants were asked to once again fill up the PANAS scale, cyber-sickness, as well as AttrakDiff 2 [15].

5 Results and Discussion

The first objective of the research was to discover whether it is possible to reduce negative emotions through virtual music therapy. To this end, we started by analyzing the emotions from the participants before, during and after the virtual MT immersion. This was done using the measurement of frustration extracted from the Emotiv EEG. Results show that the mean frustration level before the music therapy was 0.69. The mean frustration level during the immersion was 0.45. After the MT, the mean frustration level was 0.51 (Fig. 2).

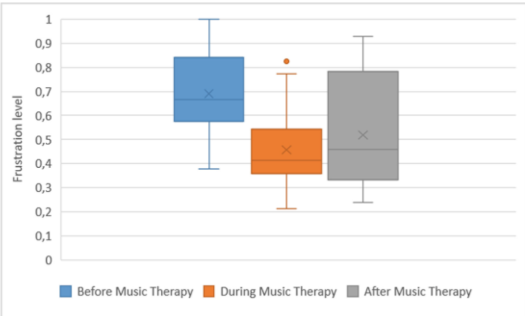

Fig. 2. Boxplot of general mean frustration

Overall, the frustration decreased when the participants were in the MT, and the positive effect on the frustration level was still observed after the MT.

The effect obtained in our first analysis lead to our second research question: is it possible to improve memory and cognitive functions through adaptive virtual music therapy? To this end, we analyzed performance improvements on the attention and memory exercises. Results showed small improvements on two of the three attention exercises. On exercise 1, the general mean improvement was 6.59%. On the second exercise, there was a mean improvement of 1.91%. The performance improvement on the third exercise was 3.51%. For the fourth exercise (first memory exercise), a mean improvement of 6.14% was observed. For the fifth exercise, the mean improvement was 8.95%. Finally, the sixth exercise showed the highest improvement, reaching 36.84% improvement. Finally, we compared improvement in attention exercises with the memory exercises. These results show a large increase in memory performance following the adaptive virtual music therapy and only a small improvement in attention abilities (Fig. 3).

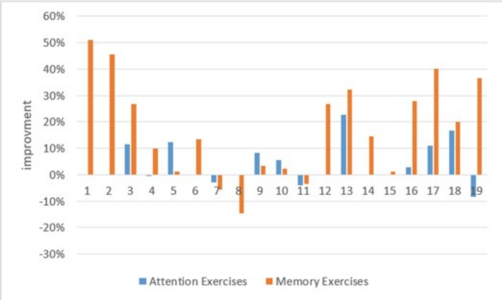

Fig. 3. Histogram of performance improvement attention compared to memory exercises.

Our first analysis confirmed that the virtual MT reduces negative emotions such as frustration. Our second and final analysis showed that reducing negative emotions through MT improved memory performances.

6 Conclusion

In this paper we presented a novel approach which could be used to improve the memory performance of subjective cognitive decline patients using adaptive virtual music therapy. Experiments were conducted during which the participants were first asked to perform attention and memory exercises, then were immersed in the music therapy environment in order to reduce negative emotions before completing a final set of exercises. The environment was built to react dynamically to the patient's emotions and change accordingly. Results showed that the virtual music therapy environment helps reduce negative emotions, most notably frustration. In addition, results showed improved memory performance on selected exercises in most participants. We speculate that the reduction of negative emotions entailed by the adaptive music therapy environment helped improve short-term memory.

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Appendix C: Journal Article 1

Paper Published in the Journal of Biomedical Science and Engineering:

EEG Analysis of the Contribution of Music Therapy and Virtual Reality to the Improvement of Cognition in Alzheimer's Disease

Journal

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Author Contributions

Researchers at Université de Montréal

Hamdi Ben Abdessalem: Integration and testing of the virtual environment. Development of cognitive exercises. Performing experiments with participants at IUGM. Results
analysis.

Claude Frasson: Development of idea to a feasible product. Supporting, funding and reviewing the research.

Alexie Byrns: Development of the virtual environment. Development of BRS theory.

Researchers at Institut de Gériatrie de l'Université de Montréal

Marc Cuesta: Performing experiments at IUGM. Reviewing paper.

Marie-Andrée Bruneau: Performing experiments at IUGM. Reviewing paper.

Sylvie Belleville: Performing experiments at IUGM. Reviewing paper.

https://www.scirp.org/journal/jbise

J. Biomedical Science and Engineering, 2020, Vol. 13, (No. 8), pp: 187-201

EEG Analysis of the Contribution of Music Therapy and Virtual Reality to the Improvement of Cognition in Alzheimer's Disease

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Keywords: Alzheimer's Disease, Brain Assessment, Virtual Reality, Music Therapy, Neurofeedback, Memory, Cognition

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ABSTRACT

Alzheimer's disease is the most common form of dementia, affecting nearly 9.9 million new people every year. The disease provokes important memory and cognitive impairment, eventually causing individuals to forget their loved ones and rendering them completely dependent on their caretakers. Alzheimer's patients typically experience more negative emotions, such as frustration and apathy, than healthy older adults. There is currently no cure for the disease. Our research group explores how the integration of virtual reality (VR) and an EEG-based intelligent agent in music therapy can alleviate psychological and cognitive symptoms of the disease. We propose a theory explaining how, through activation of the brain reward system, music can reduce negative emotions, increase positive emotions and as a result increase performance on cognitive tasks. The results of our experimental study concord with our theory: emotional states of participants are improved, as per rec- orded through EEG, and performances on memory tasks show improvement following the intervention. We believe that the combination of EEG brain assessment, VR and music therapy is a promising method for emotional states and cognitive symptoms of Alzheimer's disease.

1. INTRODUCTION

Elvis Presley, Céline Dion, The Beatles and so many others have contributed to our lives in one way or another, be it by shaping society or our simply by serenading us to work on the radio. Even though it serves no apparent evolutionary purpose or means to survival, music has persisted through time in every known culture [1]. Music no doubt is an integral part of our lives. In addition to music being a ubiquitous art form and cultural activity, it contributes to both our emotional and physical well-being in more ways than one. Evidence suggests that music can have a positive effect on a variety of diseases and disorders, including Alzheimer's disease (AD) [2, 3].

AD is the most common form of dementia and is characterized by memory and cognitive impairments. Memory is the first to be affected, where individuals often report having more difficulty remembering certain things than usual. Alzheimer's disease is progressive and its earliest phase is characterized by a state of subjective cognitive decline (SCD). While some persons with SCD stagnate, persons with SCD are at a greater risk of progressing to the disease.

No cure has yet been found, though some pharmacological interventions may reduce the symptoms. As patients progress through later stages of the disease, apathy—the lack of motivation—settles in, and patients become seemingly emotionally unresponsive [4]. This emotional state may be a hinderance to the already impaired cognitive state of patients. Indeed, a recent study showed that decreasing negative emotions in AD patients promotes better cognitive performance in both memory and non-memory related tasks [5, 6]. We believe that by intervening at the emotional level, it is possible to observe a positive influence on cognitive performances including memory tasks in AD patients. We base this emotional intervention on the integration of music therapy in virtual reality (VR), as both approaches have already proven to increase emotional well-being in AD patients [7, 8].

Many studies have investigated the relationship between music and the emotional response it generates. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies have identified correlations between the music-induced sensation of pleasure and the activity of specific brain structures, including the ventral striatum, midbrain, amygdala, orbitofrontal cortex and the medial prefrontal cortex [9]. These regions are part of the brain reward system (BRS) circuitry, a network of interconnected brain structures which play a role in the sensation of pleasure and reward [10]. It is suggested that music retains its emotional influence through the recruitment of the BRS.

In this paper we present a theory by which music associated with VR could enhance cognitive functions in AD patients. We support this view through an experimental study we conducted using electroencephalography (EGG) recordings of participant's brain activity. We interpret emotional responses of the subjects through EEG measures.

The rest of this paper is organized as follows. The first section gives an overview of AD. The second section explores evidence proving music therapy's benefits for AD patients. The third section focuses on the BRS and its role with music, where we propose a new theory explaining how music could indirectly enhance memory and other cognitive functions in AD patients. The fourth section explains the importance of EEG measurements and how they can be used to track emotional responses. The following section presents the results of our study carried out on SCD patients involving music therapy, to provide support to our theory. We conclude our paper with a discussion about the link between music and cognition.

2. ALZHEIMER'S DISEASE

Alzheimer's disease is a debilitating disease affecting memory and cognitive abilities. Most people who suffer from the disease display their first clinical symptoms after the age of 70 [11]. Although some cases can be tied to genetic mutations—often the early-onset familial form—most cases are sporadic, and their cause is unknown.

The progression of the disease manifests itself through many changes at a cognitive, behavioral and psychological level. The disease can start with subjective cognitive decline (SCD), where the patient notices impairment of their memory, but it cannot be detected with formal tests and does not affect their day to day lives. Some people remain in this state for decades and never progress to AD. People who experience SCD are more at risk of progressing towards the disease than healthy older adults. Those who do progress to AD experience gradual loss of memory and cognitive abilities, characterized among other things by difficulties in problem solving, communication and visuospatial perception. As they reach the later stages of the disease, patients become entirely dependent of their caregivers, apathetic and bedridden [12].

In addition to cognitive impairment, AD patients experience diminished psychological states. Among the many symptoms of the disease, depression and apathy are arguably the most common [4, 13, 14]. Studies show that AD patients often become anxious and uninterested in things that used to bring them joy [4]. Regularly having a negative emotional state is a common in AD patients [15], and this may aggravate the already-impaired cognitive state of patients.

On a pathophysiological level, AD is characterized by three major abnormalities: 1) brain atrophy of specific regions, 2) extracellular amyloid plaques, and 3) neurofibrillary tangles (NFT). AD brains reveal substantial neuronal death. The gyri and sulci which give the brain its distinct shriveled appearance are narrowed and widened, respectively. The ventricles also suffer from this neuronal death, becoming much larger than those of a healthy brain. At the extracellular level, Aβ amyloid plaques are found surrounding the neurons. These deposits are formed by the aggregation of amyloid β proteolytic fragments and cause disruptions in cell-cell communication. At the intracellular level, neurons display cytoskeleton abnormalities, most notably the accumulation of NFTs. These are the result of abnormal proteins which, when in their healthy form, contribute to intracellular transport, especially in the axons [16]. By bringing about disturbances in the axonal transport, tangles impair synaptic stability and eventually cause the death of the neuron [11].

Many studies have been conducted in hopes of curing the disease. Although no research has been successful, these years of research have helped better understand the disease, bringing us closer to understanding its earliest phases. While many research groups still focus on potential pharmacological interventions, a growing number of studies have begun to investigate the potential of non-pharmacological interventions in the reduction of cognitive decline and other symptoms of the disease. These interventions, which range from visual arts and music, to physical activity and electromagnetic stimulation, have proven to be promising avenues. Either on their own or by combining them with pharmacological interventions, non-pharmacological interventions are worth further investigating. In this line of thought, we explore the potential of music therapy for SCD patients.

3. MUSIC THERAPY FOR ALZHEIMER'S DISEASE

Music is a highly salient emotional stimulus. It easily generates emotions which can cause changes in mood. While providing no evolutionary advantage or association to survival, music has persisted through time as an activity providing pleasure, either when actively created or when passively listened to. Its strong ties to the triggering of emotional responses, sometimes even of involuntary movements such as swaying to the beat [17-19], may have contributed to its persistence.

Studies show that music causes positive changes in psychological and behavioral states. AD patients are no exception to this. Indeed, music can improve overall well-being, relations with caregivers, and decrease unwanted negative symptoms of the disease such as agitation, stress, anxiety and depression [8, 20-22]. Following a music therapy session, mild-AD patients generally experience an increased state of happiness and a decreased state of sadness [23].

Music also shows great potential for neurological rehabilitation. Interestingly, musical memory is partly spared even in very late stages of the disease, while other memories have become severely impaired. In terms of non-musical-related memories, reports show slowed cognitive decline [24], improved orientation, as well as enhanced memory and other cognitive functions [8, 25, 26] following music therapy sessions in AD patients.

4. THE BRAIN REWARD SYSTEM

The brain reward system (BRS) is a group of interconnected brain structures, which play a role in the rewarding experience of stimuli. These stimuli can be anything with a positive value, such as sex, food and music. When such a stimulus appears, the reward system is activated, activating the circuitry and in turn giving the subjective experience of pleasure and reward [27].

The BRS is composed of structures connecting the midbrain, limbic system and prefrontal cortex. Key structures of this network include the ventral tegmental area (VTA), amygdala, and nucleus accumbens. Within its circuitry, dopamine is the main neurotransmitter, where it is both synthesized—largely by the VTA and released. Other types of neurons, such as inhibitory neurons, play a key role in the reward circuitry by regulating neuronal activity. Incorrect regulation of the pathway can result in certain diseases and disorders, such as depression, schizophrenia, addiction and Parkinson's disease [28].

The BRS plays an important role in the processing of emotional stimuli and certain memory functions. Lesions of the amygdala, a structure of this network, have shown to impair implicit memory: a type memory that stores knowledge unconsciously acquired. Lesions of the amygdala can therefore cause impairments in the unconscious recall of both perceptual and motor skills [11].

As mentioned earlier, BRS-activating stimuli can be many things. Indeed, music has repeatedly shown to activate structures related to biological reward [3, 29-31]. It is proposed [32] that music activates the BRS through interaction between cortical networks related to audition and to reward.

Activation of the reward system through music has been shown to maximize pleasure by increased activation in of specific brain structures and decreased activity in structures associated with negative emotions through inhibitory activity towards other specific structures [9]. In addition to its ties with emotional state, some studies link the BRS to certain cognitive functions. Notably, a study showed that short exposure to rewarding stimuli reduced cortisol, a so-called stress hormone, and resulted in better problem-solving performances in stressful situations [33]. Other studies also show that lesions of the amygdala have led to impaired implicit memory [11], suggesting that the BRS plays a role in the recollection of implicit memories.

Considering these previous findings, **we propose the following theory: By increasing positive emotions and reducing negative emotions through the activation of the BRS, music improves cognitive functions of SCD participants. We divide this hypothesis in two research questions: 1) Does virtual music therapy increase positive emotions and decrease negative emotions? and 2) Does the virtual music therapy increase cognitive functions?**

5. OUR EXPERIMENT: MUSIC THERAPY VIRTUAL ENVIRONMENT

5.1. Brain Assessment: Analysis through EEG

In the brain assessment field, many studies use physiological sensing approaches such as electroencephalography (EEG) to detect and analyze emotional states. By being readily available, inexpensive and non-invasive, EEG is a simple and easy way to get an inside view of subjects' brain activity. Through the analysis of the electrical activity emitted from the brain, researchers can better understand the inner workings of the brain.

Using EEG has not only proven to be beneficial for research, but has also showed to benefit participants themselves. A study showed that by using the assessment of engagement and frustration, appropriate help strategies could be provided to participants engaged in a physics-related game [34]. Furthermore, it has been shown that a positive mental state promotes better learning in students. Taking this into account, Chaouachi *et al.* [35] developed a system based on EEG-recorded engagement and workload to help keep students in a positive mental state.

By using EEG recordings, we aim to get an inside view of our participants' emotions. Using the real-time-provided emotional state, we can create an intervention better adapted to the participant. EEG headsets have shown to be well tolerated by SCD subjects [5, 6].

In our study, we use the Emotiv Epoc EEG headset to track emotions. The headset contains 14 electrodes spatially organized according to the International 10 - 20 system, moist with a saline solution. The electrodes are placed in antero-frontal (AF3, AF4, F3, F4, F7, F8), fronto-central (FC5, FC6), parietal (P7, P8), temporal (T7, T8) and occipital (O1, O2) regions with two additional reference sensors placed behind the ears. The detailed position of the measured regions is shown in **Figure 1**.

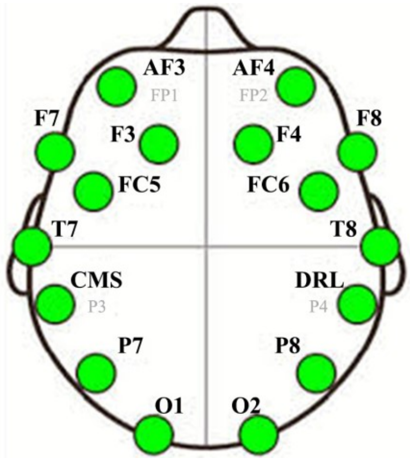

Figure 1. Emotiv headset sensors placement.

The Emotiv system generates raw EEG data (in μV) with a 128 Hz sampling rate as well as the five well-known frequency bands, namely Theta (4 to 8 Hz) Alpha (8 to 12 Hz), low Beta (12 to 16 Hz), high Beta (16 to 25 Hz) and Gamma (25 to 45 Hz). Furthermore, the system uses internal algorithms to measure the following mental states: meditation, frustration, engagement, excitement and valence.

Although we don't have access to the system's proprietary algorithms to infer these mental states, a number of studies have provided evidence showing the reliability of its output [36].

5.2. The Virtual Environment

Our music therapy was designed within a virtual environment. This modality was chosen based on three main factors. For one, the application of VR in a wide range of psychiatric disorders has shown its potential and proven its usefulness [37]. Studies using VR on AD patients have shown that participants tolerated well the headsets, and even enjoyed the VR experience [5]. Secondly, the virtual environment enables for a stronger feeling of immersion and increases ecological validity. This in turn provides a stronger influence of the environment on emotional state. Finally, by pairing the virtual environment with an EEG headset and integrating an intelligent agent, the environment can evolve and adapt itself as a function of the participant's EEG readings. In an attempt to improve and optimize the utilization of VR, we propose the integration of an intelligent agent capable of modifying the environment appropriately as a function of emotions.

We designed an environment resembling a theatre using Unity 3D software. We virtually placed the participant in the center of the room, on a seat, where they could easily see the stage up front and dynamically rotate their head to visually explore the room. At the start of the session, cliché red curtains opened the stage area.

A series of eight 30 second song excerpts are sequentially presented in the following order: 1) Ave Maria by Franz Schubert, 2) Eine Klein Nachtumusik: Allegro by Mozart, 3) Ukulele by Bensound, 4) Clair De Lune by Debussy, 5) La Vie En Rose by Edith Piaf, 6) Everyday by Buddy Holly, 7) La Bamba by Ritchie Valens, and finally 8) What A Wonderful World by Louis Armstrong. Each song excerpt was clearly separated from the previous by the red curtains closing and opening. The choice of music was based on studies and theories. A portion of the songs were chosen because they contained melodies with structural features associated with anxiety reduction (*i.e.* slow tempo, low pitches) [38]. Another portion of the songs was selected based on their popularity in North America during the years corresponding to our participant's reminiscence bump. This refers to a time period where events and memories are more likely to be remembered. The reminiscence bump corresponds to the time between the ages of 10 and 30, with the likelihood of remembering events peaking around the age of 20 years old [39]. Given that the mean age of our participants was 72, some songs we selected reached the billboard charts between the years 1957 and

1977.

For each song, the stage displayed a selection corresponding instruments, each slightly animated, as well as firework-like visual effects (see **Figure 2**). The intensity of the light as well as the colors of the visual effects was chosen as a function of the emotional purpose of the song. Scenes were designed with specific shades of red, purple, blue, green and yellow, as these are suggested to be the most pleasant and arousing hues [40].

Once the eight song excerpts were done, the environment was adapted to provide the most beneficial therapeutic experience to each individual participant. This was calculated based on the participants' emotional response analyzed though EEG recordings. Indeed, different songs and different visual effects can have varying impacts on individuals.

In order to best suit each participant, we used a method with a neurofeedback agent: Neurofeedback is a type of biofeedback that measures brain waves to produce a signal that can be used as feedback. When the measured activity is cerebral activity, biofeedback is called neurofeedback [41]. The neurofeedback agent tracks the emotions of the participants while they listen to the eight songs, detects the song which provokes the best emotional impact and plays this song once again for a longer period of time. Using this neurofeedback approach, we finally adapt the playlist to the user in order to favorize the song which has the most potential effect on the participant. This means the song that has less negative effect and most positive effect on the participant's emotional state. The neurofeedback aspect of our environment enables to optimize the emotional impact for every individual participant.

5.3. Experiments

In order to study the impact of the music therapy environment on attention and memory performances, we created 6 attention and memory exercises using Unity 3D software. The following provides brief descriptions of each exercise.

5.3.1. Attention Exercises

For the first attention exercise, the participant hears a series of numbers and is invited to replicate the sequence in the same order as presented using a numerical pad. Then, another series of numbers is presented but the participants are now invited to report numbers in the reversed order. **Figure 3** illustrates how the participant uses the numerical pad in order to interact with the exercise.

For the second attention exercise, participants hear a series of letters (one letter per second) and are required to click on the space bar of the keyboard each time they hear the letter "A".

Finally, in the third attention exercise, participants are shown pictures of different items for a short period of time. Then, after each picture, four letters are presented and they are asked to select the letter corresponding to the first letter of the presented item's name.

5.3.2. Memory Exercises

For the first memory exercise, we present several objects visually or aurally to the participants and ask them to memorize them. After that, we present a series of objects and the participants are asked to select whether the object was seen, heard or never presented. **Figure 4** shows the case where the participant answers they have seen the image of the car.

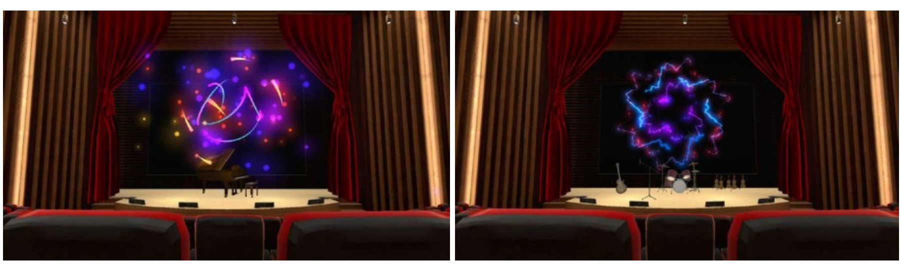

Figure 2. Scenes for two different songs from the virtual environment.

Figure 3. Screenshot of attention exercise 1.

Figure 4. Screenshot of memory exercise 1.

For the second memory exercise, we present several circles spread out against the virtual wall. Then, a series of circles is highlighted one by one in order to create a sequence. The participants are invited to memorize and repeat the same sequence.

Finally, in the third memory exercise, we ask the participants to memorize sets of three pictures for a short period of time. Then, we present four sets of three similar pictures to the participants, and they are asked to select the set matching the one that was previously presented.

5.3.3. Experimental Process

We tested our approach on 19 participants (13 females) with subjective cognitive decline (SCD) and a mean age = 72.26 (SD = 5.82). In order to ensure that the participants were eligible for the study, they had to pass through a pre-experimental session. In this session, participants were presented with oral and written descriptions of the study and were invited to sign a consent form. Then, they performed the clinical tests necessary to confirm diagnosis of SCD and characterize them. Only the eligible participants were invited to the experimental session.

In the experimental session, participants were first invited to fill the following questionnaires: The Positive and Negative Affect Schedule (PANAS) scale [42], a self-assessment of emotions, and a questionnaire on cyber-sickness [43]. Then, we equipped the participants with an EEG headset and invited them to start solving the attention and memory exercises. Following these tests, participants were equipped with a FOVE VR headset, and the VR music therapy environment was launched. The relaxation environment lasted for about 10 minutes. Following the virtual environment, participants completed different variants of the same attention and memory exercises. Finally, the experimental session came to an end after asking the participants to once again fill the PANAS scale, cyber-sickness, AttrakDiff 2 [44] and a self-report form about the environment. **Figure 5** shows the steps of the experimental process.

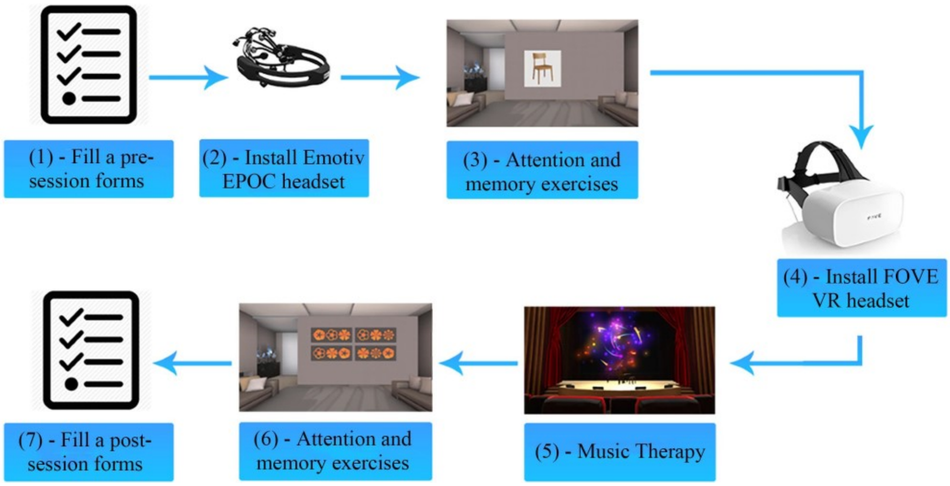

Figure 5. Process of the experiment.

6. RESULTS

Our first research question asked: **Does virtual music therapy increase positive emotions and decrease negative emotions?** To this end, we started by analyzing the emotions of the participants before, during and after the virtual music therapy immersion. This was done on the measure of frustration and valence extracted from the Emotiv EEG recordings. Results show that the mean frustration level before the music therapy was 0.69 (0.37 minimum and 1.00 maximum). The mean frustration level during the immersion was 0.45 (0.21 minimum and 0.82 maximum). After the immersion, the mean frustration level was 0.51 (minimum 0.23 and maximum 0.92). **Figure 6** shows a boxplot of the mean frustration before, during and after the music therapy session.

Overall, the frustration decreased when the participants were in the virtual environment, and the positive effect on the frustration level was still observed after the music therapy.

Next, we analyzed the mean valence before, during and after the music therapy immersion. Results show that the mean valence before was 0.59 (0.48 minimum and 0.78 maximum). The mean valence during the immersion was 0.54 (minimum 0.47 and maximum 0.65). After, the mean valence level was 0.75 (minimum 0.55 and maximum 0.92). **Figure 7** shows a boxplot of the mean valence before, during and after the virtual environment.

Overall, the valence decreased slightly when the participants were in the virtual environment but increased considerably following their immersion. We believe this is a result of the experiment's design, where the emotional optimization (choice of the song with the best emotional impact) took place at the very end of the music therapy session.

In addition, post-session appreciation forms revealed that 89.5% of the participants found that the environment was immersive while 5.3% reported that the environment was not immersive, and the rest gave a neutral response. Results also showed that 84.2% of the participants reported that the virtual reality had a positive impact on their user experience, 5.3% reported that the virtual reality had a negative impact and the rest gave a neutral response. Finally, 89.5% of the participants reported that they liked the environment and they found it relaxing, 5.3% reported that it was not relaxing, and the rest gave a neutral response.

Thus, the music therapy environment reduced negative emotions, such as frustration, and increased positive emotions, like valence and relaxation. This observation led to our second research question: **Does the virtual music therapy increase cognitive functions?** To this end, we analyzed performance improvements on the attention and memory exercises of each participant. We begin by presenting the results of the attention exercises and follow with those of the memory exercises.

For the attention exercises, results show small improvements. For the first exercise, the general mean improvement was 6.59%. For the second, there was a mean improvement of 1.91%. The performance improvement on the third exercise was 3.51%. More detailed results are shown in **Figure 8**, where we note that for exercise one, 6 participants showed improvement, 3 decreased performance and the rest maintained the same performance. On the second exercise, 3 participants showed improvement, 1 decreased performance and the rest held the same performance. Finally, on the third exercise, 5 participants showed improvement, 2 showed a decrease of performance and the rest kept the same level of performance.

More desirable improvement levels were observed with regards to the memory exercises. For the fourth exercise (first memory exercise), a mean improvement of 6.14% was observed. For the fifth exercise, the mean improvement was 8.95%. Finally, the sixth exercise showed the highest percentage of improvement, reaching 36.84%.

Individual results are shown in **Figure 9** where we can see that for the fourth exercise, 7 participants showed improvement, 3 experienced decreased performance, and the rest kept the same performance. For the fifth exercise, 11 participants displayed improvement, 7 had a decrease of performance, and the rest kept the same performance. Finally, for the sixth exercise, 12 participants showed improvement, 2 had decreased performance and the rest kept the same level of performance.

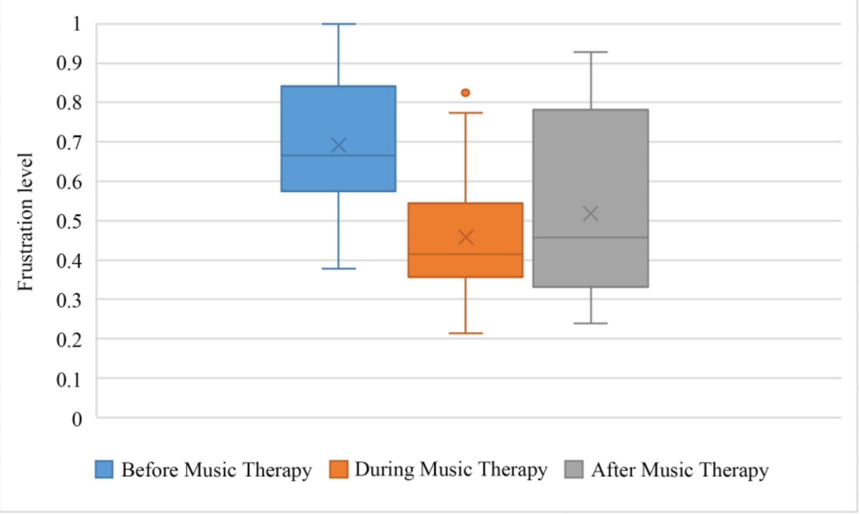

Figure 6. Boxplot of general mean frustration.

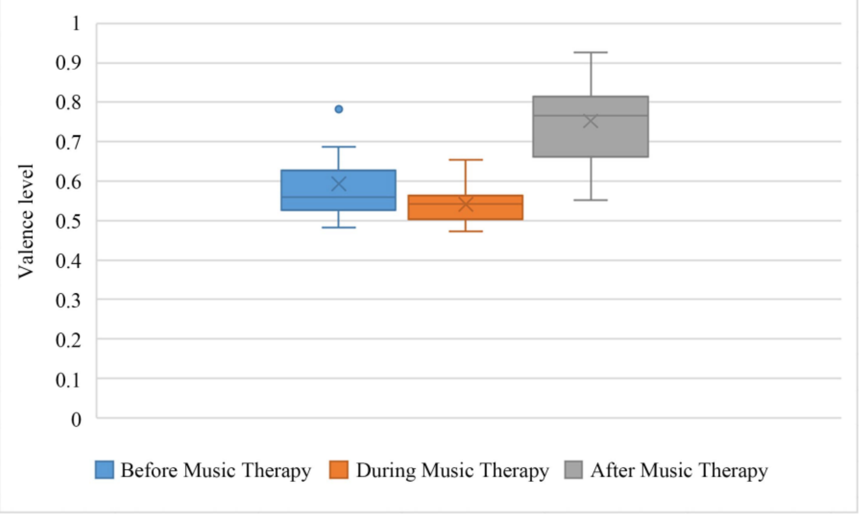

Figure 7. Boxplot of general mean valence.

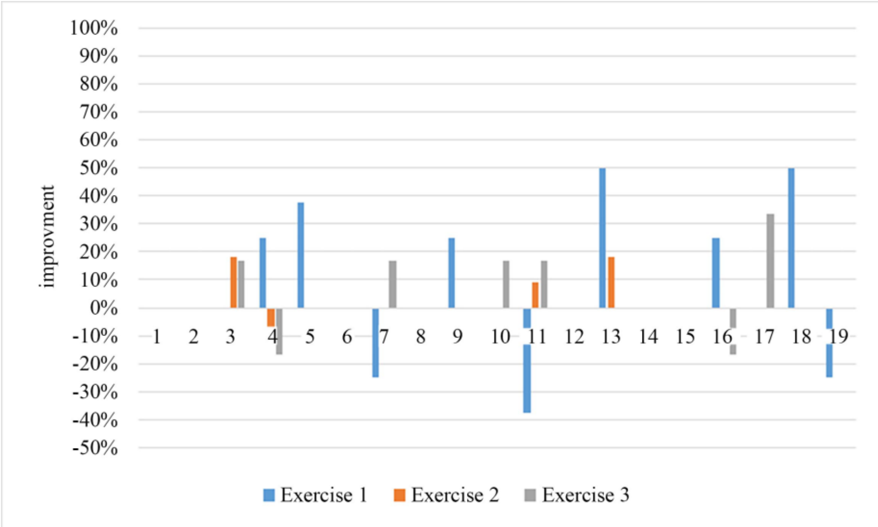

Figure 8. **Histogram of performance improvement in attention exercises (1, 2 and 3).**

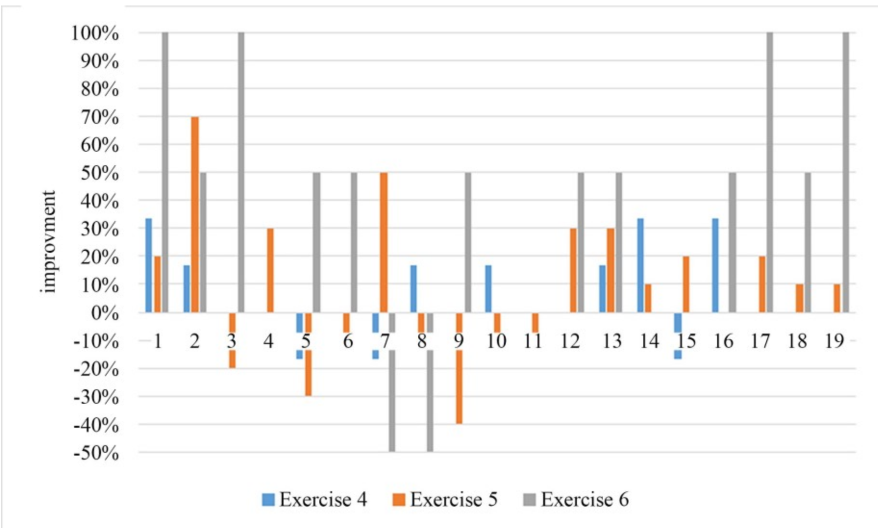

Figure 9. **Histogram of performance improvement in memory exercises (4, 5 and 6).**

These results show a considerable **increase in memory performance** following the adaptive virtual music therapy and only a small improvement in attention abilities.

7. DISCUSSION

In this paper, we develop a theory explaining how music therapy can enhance cognitive functions. Our experimental study aimed to identify the emotional and cognitive impact of a virtual music therapy environment on people suffering from subjective cognitive decline (SCD). Results of the study showed that following the intervention, both emotional state and cognitive performance was improved for most participants. Our results are, at first view, in accordance with our hypothesized theory, which was: **By increasing positive emotions and reducing negative emotions through the activation of the brain reward system (BRS), music improves cognitive functions.**

The first research question considered that music would activate the BRS and thus influence the emotional state of the participants. As this has already proven to be the case through many studies and was explored in a previous section, it was unsurprising to observe changes in emotional states of participants as they listened to the different songs. In general, negative emotions were reduced, as observed through the measure of frustration, and positive emotions were increased, as seen through the measure of valence. Following the experiment, a large majority of the subjects reported having enjoyed the session. In concordance with the literature [9, 45, 46], we believe this emotional change is a result of the activation of the BRS.

The second research question asked if the positive change in emotional state would result in better memory and attention performances. Our experimental results show a clear improvement in memory performance for most participants and a small tendency for improvement in attention performance. We propose that these increases in performance are a result of the change in emotional state generated by the music therapy. Although we do not have a direct physiological measurement proving causation from the emotional state to the cognitive state, many studies have shown strong correlations between emotions and mental states. For example, frustration is tightly tied to a high workload, and the inverse is also true. Reduction in workload correlates with reduced frustration [47]. Indeed, we base ourselves on the many studies which have shown correlation between better cognitive states (*i.e.* less stress, more engagement) and better performance scores on cognitive tasks [48].

Importantly, many findings have established that positive mood states enhance memory function [48]. The theory we put forth merely proposes a process by which music influences memory. We created logical links between music, the BRS and emotions to explain how music influences cognitive functions. Through EEG analysis and cognitive performance assessment, the results of our experiment are in line with our theory.

Our results show that the neurofeedback agent was indeed effective in choosing the appropriate song to play at the end of the intervention. As targeted, negative emotions were reduced, and positive emotions were increased following the virtual experience. The intelligent agent successfully improved emotional states.

Interestingly, the mean valence decreased during the music therapy session, and was followed by an important increase post-session. We believe this is due to how the virtual music therapy session was designed: for the first and longest part timewise, eight different songs are presented, some of which could have given rise to negative emotions. For example, one might have associated "Ave Maria" to the song played at someone's recent funeral, generating negative emotions. The second and final part of the intervention was reserved to play the song which most improved the emotional state of the participant. For this reason, we believe the overall valence during the experienced decreased slightly, and the post-session valence was greatly increased due to the last, optimized song, having the most influence on the post-session emotional states.

Our results show a noticeable difference between the performance improvements of the memory and the attention tasks, with the memory improvements exceeding those of the attention improvements. We propose that this is due to facilitated memory access generated by music. As mentioned in an earlier section of this paper, the amygdala, a structure part of the BRS, is an important player in emotional processing and implicit memory. A study describes how emotional context associated with music and its saliency may lead to preserved residual memory functions in AD. They propose that since music is a salient emotional stimulus, it could potentially facilitate the access to the amygdala-based network and in turn provide better memory functioning [3]. This could explain why our participants experienced a small increase in attention performance and a larger increase in memory performance.

In summary, our experimental study provides support to our theory, which proposed that music helps cognitive functions through the activation of the BRS which provides a better mental environment for cognitive tasks. Future research should investigate through different imaging techniques the activation of the amygdala during music therapy sessions and memory tasks.

8. CONCLUDING REMARKS

The aim of this paper was to introduce and support a theory by which music can enhance cognitive functions in Alzheimer's disease. We propose that the pleasurable experience of music is directly tied to the activation of the brain reward system; a network of interconnected brain structures was involved in dopaminergic activity and in turn the rewarding and motivational experience. The activation of these pathways leads to increased release of dopamine and therefore the subjective experience of pleasure in the listener's brain. This uplift in emotional state can be linked with better cognitive performances, as suggested by various studies in the fields of neuroscience and computer science's intelligent tutoring systems. We explore this theory through a study we conducted on people suffering from subjective cognitive decline. Results show that following the music therapy session, participants had increased positive emotions, reduced negative emotions, slightly increased attention performance and increased memory performance. Supporting our theory, we propose that the cognitive performance increase is a result of a better cognitive environment generated by the music. We propose that by activating the reward system—increasing the dopaminergic release—and in turn generating positive emotions, music can positively affect memory and other cognitive functions.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix D: Conference Article 3

Published Paper in 16th International Conference on Intelligent Tutoring Systems, 2020:

Improving Cognitive and Emotional State Using 3D Virtual Reality Orientation Game

Conference

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Author Contribution

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Manish Kumar Jha: Support developer of VR environment. Developed idea of using hints to help participants to solve the tasks. Developed rule-based guidance system and improvement using reinforcement learning. Integration and testing of the developed product. Analysis of results.

Marwa Boukadida: Main developer of the VR environment. Performing the experiments with participants at IUGM.

Hamdi Ben Abdessalem: Support developer of VR environment. Integration and testing of the developed product. Development of memory and attention exercises. Performing the experiments with participants at IUGM. Analysis of results.

Claude Frasson: Development of idea to a feasible product. Supporting, funding and reviewing the project.

Alexie Byrns: Original abstract idea of using cognitive maps in orientation-based games as cognitive exercise.

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Marc Cuesta: Performing experiments at IUGM. Reviewing paper.

Marie-Andrée Bruneau: Performing experiments at IUGM. Reviewing paper.

Sylvie Belleville: Performing experiments at IUGM. Reviewing paper.

Improving Cognitive and Emotional State Using 3D Virtual Reality Orientation Game

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Abstract. Patients suffering from Alzheimer's Disease (AD) exhibit an impairment in performing tasks related to spatial navigation. Tasks which require navigational skills by building a cognitive map of the surrounding are found effective in cognitive training. In this paper we investigated the effect of cognitive training using a fully immersive 3D VR orientation game. We implemented an intelligent guidance system which helps to reduce the negative emotions if the participants experience difficulty completing the quests of the game. We found that after playing the orientation game, participants performed better in memory and in certain attention exercises. We also studied the effects of guidance system to reduce the frustration during cognitive training using VR environments.

Keywords: Virtual Reality · Orientation · EEG · Immersive environment · Game adaptation · Assistance system

1 Introduction

The ability to find one's way using spatial reference frames and cues from our surrounding is a complex cognitive process. Studies show that navigational skills decline with ageing [1]. However, people with Alzheimer's disease (AD) display a significantly higher decline, which is also one of the early symptoms of the disease. Research shows that spatial navigation training programs in older persons led to improvements in spatial performances [2].

Virtual Reality (VR) applications can be used to address the challenges of cognitive training of dementia patients due to a high level of interaction possible within a virtual environment (VE) without being in any risk otherwise posed by real-life surroundings. In this paper, we present a fully immersive VE where the participant must find items of interest in a public garden. However, navigating in an unfamiliar place can be challenging, consequently leading to higher negative emotions and a tendency to give up

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https://doi.org/10.1007/978-3-030-49663-0_26

before completing the experiment. Research shows that it is more beneficial for patients with cognitive impairment to be helped through the completion of a challenge, rather than see the challenge failed [3]. It is important to present both audio and visual cues to cater to the needs of a specific profile of patients suffering from either visual or auditory impairments [4]. Thus, real-time assistance with audio and visual feedback is one of the mandatory components in games for elders, to incorporate mechanism which achieves high-level engagement by keeping player filled with positive emotions. Hence, we implemented an intelligent guidance system based on participant's behavior, that helps them to complete the tasks without being explicitly asked for help.

Our goal for this study is to investigate the effect of the orientation game and the guidance system on the cognitive functions of people suffering from subjective cognitive decline (SCD), a preclinical state of possible Alzheimer's Disease (AD). We state our research objectives as the following: Q1: is it possible to stimulate the brain using a virtual maze game in order to enhance attention and memory? Q2: is it possible to help participants in order to reduce negative emotions?

The rest of this paper is organized as follows. In Sect. 2, we discuss the related works and the cognitive map theory. In Sect. 3, we describe the orientation game: the environment, the objectives and the guidance system. In Sect. 4, we detail the cognitive tests and the experimental procedure undertaken to validate our hypotheses. Finally, in Sect. 5 we present and discuss the obtained results.

2 Related Works

According to the cognitive map theory, the formation of representations of spatial information – in other words, the creation of a cognitive map – helps reduce cognitive load and increases recall and the encoding of novel information [5, 6]. Studies report that decreases in the volume of the hippocampus – a structure playing a key role in memory – correlate with a decline in cognitive function. Indeed, it is speculated that increasing grey matter in the hippocampus could entail better memory [7]. Interestingly, playing 3D video games over a period, such as Super Mario 64, reportedly increases hippocampal volume [8], as well as increases performance in episodic and spatial memory quests. It is speculated that 3D games, such as Super Mario 64, lead players to create a cognitive map of the environment.

It has been observed that virtual reality environments (VE) lead to formation of cognitive maps similar to the real environments [9]. This makes VR games ideal for simulating real life scenarios for cognitive training of elderly. Certain VR applications have concentrated on games focused on performing activities of daily life such as cooking, driving and shopping [10]. Another key advantage of using VE is that they offer a safe way to achieve high level of interaction adaptable to the characteristics and needs of individual patients [10, 11]. A fully immersive VE offers higher sense of 'presence' and interaction which subsequently affects the behavioral responses of patients.

3 Orientation Game

3.1 Environment: Orientation Game

The fully immersive VR environment simulates a botanical garden in the form of a 5×5 maze. In this environment, trees form the walls of the maze and clearings through the trees are the pathways. The participant starts at one end of the garden and has to navigate using a joystick by clicking in the direction in which he/she intends to move. Other elements in the game are: 1) a map of the garden with geographical directions, 2) the position and direction of the user shown by a red arrow in the map, 3) a flashing blue circle representing the location of the items, 4) visual hints displayed when needed and, 5) verbal messages to the participant.

The game starts with a tutorial to let the users familiarize themselves with the environment and the controls. It consists of four quests. For the first three quests, the participant is asked to collect an item located at a specific location of the 5×5 maze. We display the name of the item and its location by a flashing blue circle on the map for 5 s. The user needs to reach the location and collect the requested item. When the item is collected, we remove it from the list and display the next item and its location.

3.2 Guidance System

We implemented a rule-based guidance system that provides navigational hints or audio and visual messages to the participants and helps them in completing the quests. It actively monitors the participant's emotions, namely frustration, excitement, engagement, meditation, and valence using Emotiv electroencephalograph (EEG) headset data in real-time. On sensing a situation where the participant may need a hint, it sends a message to the VR system, which displays the hints in form of location in the map or audio and visual messages in case of text-based hints. Figure 1 shows the different hints provided by the guidance system.

Hint levels		**Participant's position**	**Object's location**	**Message (Audio and Visual)**	**Highlighted Path in Map**
Level 1		✓	✓		
Level 2	**2-1**	✓	✓	*Please check the position of object on the map.*	
	2-2	✓	✓	*You are too far. Try to take few steps back.*	
	2-3	✓	✓	*1. Good job! Almost there.* *2. Keep up the good work* *3. You are going in right direction*	
Level 3		✓		*Follow the displayed path. The object is somewhere nearby.*	Path to cell nearest to target object
Level 4		✓		*Follow the given path to find the object*	Complete path to the object.

Fig. 1. Different level of hints

The hints provided by the guidance system are activated in three different cases:

1. Emotions: At every second, the mean of the change and the rate of the change of emotion values in past ten seconds are used to calculate a net score for each

emotion. The emotion with the maximum score is compared with an empirically defined threshold to activate the emotion-based hints.
2. Away from target: If the participant takes three steps or more, all of which are at four blocks or more from the target, the map displaying target location is activated.
3. No Movement: If the participant doesn't move for more than a given amount of time, the map displaying target location is activated.

The details change with different levels of hints provided by the guidance system. Level 1 provides the least information and displays only the participant's location and the object's location on the map. Additionally, level 2 displays a text message in a prompt in the VR environment along with the verbal narration of the message. Level 3 hint highlights a path in the map, which the participant can follow to reach a location immediately next to the actual location of the object. This leaves some scope of exploration and the participant needs to search for the object in all possible directions. Level 4 hint highlights the complete path leading to the object's location on the map.

In case of activation based on participant's emotion, if the hint is triggered by frustration, the level of hint increases which provides more details to find the object. On the other hand, if the hint is triggered by positive emotions such as excitement or engagement, the level of hint decreases. In case of hint activated due to no movement of the participant, the level increases every fifteen seconds till the participant moves. When the participant is away from the object as determined by the guidance system, the hint provided is always level 2-1.

4 Experiments

Since our main goal is to analyze the impact of orientation therapy and building a cognitive map on the attention and memory performances, we developed 3 attention exercises and 3 memory exercises to compare participants' performances before and after playing the game. We tested our approach with 15 participants (11 females) with subjective cognitive decline (SCD) and a mean age = 73.4 (SD = 5.73).

The participants took part in two sessions. In the first session, we performed some assessments to ensure that they were eligible to conduct the experiments. During the second session (experimental session), the participants were invited to fill a pre-experiment form. Afterwards, we equipped them with an EEG headset, and they start resolving attention and memory exercises. When they complete the exercises, we equip them with Fove VR headset, and they start the Orientation Game. Following the game, we removed the Fove VR headset and the participants were asked to complete the attention and memory exercises again but with different examples. Finally, we remove the EEG headset and the fill up a post-experiment form.

5 Results and Discussion

In order to study the enhancement in attention and memory, we analyzed performance improvement before and after the orientation therapy of the first three exercises (Attention exercises). On exercise 1, the general mean improvement was 6.67%. on the second exercise, there was a mean improvement of 0.61%. And the performance improvement of the third exercise was 0%. We also analyzed the performance improvement before and after the orientation therapy of the memory exercises (exercise 4, 5 and 6). For the fourth exercise, the mean improvement was 1.11%. For the fifth exercise, the mean improvement was 12%. Finally, the mean improvement is 26.67% for exercise 6 which is the highest percentage of improvement. These results show increase of memory performance following the orientation therapy and an improvement in attention abilities in certain participants.

Next, we analyzed the frustration of the participants before and after the hints are provided. As shown in Fig. 2, the guidance system provided at least one or more hints to 9 out of the 15 participants. In the rest of the cases, participants didn't have any difficulty in completing the quests.

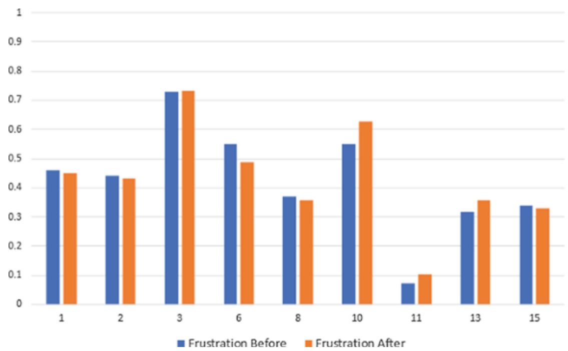

Fig. 2. Average values of frustrations of each participant, ten seconds before and after the hints

We notice that in 6 out of 9 participants, frustration values in next ten seconds decreased for the hints provided to them. Participants 8, 10, 11 and 13 were respectively provided one, two, one, and one hint, while the rest of the participants received at least five or more hints. For the different types of hints, we observed that except for hint level 2-2 and hint level 4, the average values of frustration for all the participants were lesser in the next ten seconds after the hints were provided. Hint level 2-2 provides a warning message: 'You're too far. Try to take few steps back.'. This led the participants to believe that they might be doing something wrong leading to higher frustration. Hint level 4 displays the complete path to the item's location. But, since we configured the hint to appear for only four seconds, it was not enough for the participants to memorize the complete path, which may lead to a more frustration.

6 Conclusion

In this paper, we designed a 3D VR orientation game in with real-time guidance system which can be used for cognitive training of the patients suffering from pre-clinical states of Alzheimer's disease. The results show an improvement in memory performance for most of the participants, and better attention abilities for some of the participants after the therapy. The guidance system is effective in reducing the frustration while solving quests of the game. In some cases, the decrease is not significant, but the stabilization of frustration after a continuous increase after the hint is provided shows the usefulness of hints. Also, the increase in negative emotions after two hints shows that hints need to be carefully designed to give positive messages and the time taken to understand the hints should be taken in consideration.

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Appendix E: Conference Article 4

Paper Published in 2nd International Conference on Brain Function Assessment in Learning, 2020:

Immersive Orientation Game for Alzheimer's Disease using Real-time Help System

Conference

Brain Function Assessment in Learning, 2nd International Conference, BFAL 2020, Heraklion, Greece, October 9–11, 2020

Author Contribution

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Manish Kumar Jha: Support developer of VR environment. Developed idea of using hints to help participants to solve the tasks. Developed rule-based guidance system and improvement using reinforcement learning. Integration and testing of the developed product. Analysis of results.

Marwa Boukadida: Main developer of the VR environment. Performing the experiments with participants at IUGM.

Hamdi Ben Abdessalem: Support developer of VR environment. Integration and testing of the developed product. Development of memory and attention exercises. Performing the experiments with participants at IUGM. Analysis of results.

Claude Frasson: Development of idea to a feasible product. Supporting, funding and reviewing the project.

Alexie Byrns: Original abstract idea of using cognitive maps in orientation-based games as cognitive exercise.

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Virtual Reality Orientation Game for Alzheimer's Disease Using Real-Time Help System

Chapter · October 2020

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Virtual Reality Orientation Game for Alzheimer's Disease using Real-time Help System

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Abstract. Studies support cognitive training as a potentially efficient method to postpone cognitive decline in persons with mild cognitive impairment (MCI). Virtual reality (VR) based serious games have found application in this field due to high level of immersion and interaction possible with the environment. We propose a fully immersive virtual reality 3D orientation game with real-time guidance system for training of elder adults. We studied the immediate after-effects of playing the orientation game on memory and attention abilities. After playing the game, participants performed better in memory exercises compared to attention exercises. The game was equipped with a real time guidance system to help the participants complete the tasks in the game. We noticed that certain hints which displayed positive messages or were easier to comprehend, helped in reducing frustration. On the other hand, hints which gave a warning message or were more difficult to follow, caused frustration to increase.

Keywords: Guidance System, Orientation, Game Adaptation, Virtual Reality, EEG.

1 Introduction

Spatial navigation, an application of higher cognitive functions, is a key part of human life and is essential for carrying out activities every day. Allison et al. [1] showed that early-stage symptomatic Alzheimer's Disease (AD) related deficits in the aspects of spatial navigation for the use of both wayfinding and route learning strategies. According to the cognitive map theory, the formation of representations of spatial information using spatial reference frames and cues from the surroundings, in other words, the creation of a cognitive map – helps reduce cognitive load and increases recall and the encoding of novel information [2, 3]. It has been observed that decrease in the volume of the hippocampus – a structure playing a key role in memory – correlate with a decline in cognitive function. Indeed, it is speculated that increasing grey matter in the hippocampus could entail better memory [4]. Interestingly, playing 3D video games over a period, such as Super Mario 64, reportedly increases hippocampal volume [5], as well as increases performance in episodic and spatial memory quests. It is speculated that 3D games, such as Super Mario 64, lead players to create a cognitive map of the environment.

Cognitive training on older adults suggest that cognitive training may also serve to optimize the cognitive functioning of persons with noticeable cognitive decline and contribute to a slowing of the onset of the disability [6]. It has been observed that virtual environments lead to formation of cognitive maps similar as in the real environments, despite certain limitations (misperception, cyber-sickness and disorientation) [7]. There is an increasing trend of using virtual reality (VR) games and applications for cognitive training of the elderly. A VR environment offers a safe way to achieve high level of interaction along with the possibility of performing activities, adaptable to the characteristics and needs of individual patients [8, 9]. Another key aspect of using VR for training is that it allows the collection of data in the form of biomedical signals of the participant, which can be analyzed to study and improve the effectiveness of training sessions. In terms of interaction, fully immersive VR environments using head mounted display create a more realistic sense of presence compared to non-immersive or partial-immersive environments (monitor-display) [10].

In this paper, we implemented a fully immersive 3D- VR game in which the participants use his/her navigational skills to form a cognitive map of the environment and complete the tasks within the game. The environment simulates a public garden in the form of a maze, and the tasks are to search for certain items of interest in a listed order. While the participant plays the game, the system records their EEG signals by the means of an Emotiv headset. Navigating in an unfamiliar environment can be challenging, consequently leading to increased negative emotions if the participant fails to locate the required item. Hence, we implemented an intelligent guidance system that assesses the emotions of the participants, tracks their movement in real-time, and provide hints to complete the tasks in the game.

Our objective is to explore the effect of a fully immersive VR navigation game on the performance of attention and memory capacities of patients suffering from subjective cognitive decline (SCD), a preclinical state of Alzheimer's Disease (AD). Our research concentrates on understanding if **it is possible to improve memory and attention performance through a virtual maze game.** We also explore the benefits of hints in game can in terms of change in frustration of the participants on providing hints.

The rest of this paper is organized as follows. In section 2, we give an overview of the related works. In section 3, we describe our approach. In section 4, we detail the experimental procedure, and finally, in section 5 we present the obtained results.

2 Related Works

Over the years, many studies have implemented multiple VR environments for cognitive training. In one of the earlier studies, attention enhancement in young students was observed in a VR classroom compared to non-VR control group [11]. Another study done on graduate students, observed an improved ability to recall the spatial location of objects in VR environment simulating an apartment [12]. Optale et al.[13] observed that VR memory training during a period of three months presented an improvement in long term memory in elders with memory impairment. They suggested that repeated exposure of elderly to VR based cognitive training may simulate their attention owing to high degree of immersion and interaction. In a recent work, a VR environment simulating activity of daily life (e.g. cooking) and an environment focused on memory training using autobiographical memory has been proposed [14]. Gamito et al.[15] used working memory tasks (i.e. buying several items), visuo-spatial orientation tasks (i.e. finding the way to the minimarket) in a VR environment for training of stroke patients two to three sessions per week over the four to six week period of treatment. Their study revealed a general improvement in attention and memory abilities over multiple training sessions.

Research have used physiological sensing approaches like electroencephalography (EEG) to detect and analyze mental states and emotion to assist in learning, intelligent video games etc. Ghali et al. [16] used EEG signals to assess participants' mental states and focused on their engagement and frustration. Based on these two mental states they proposed help strategies in a physics game. For the elderly, continuous feed-back and guidance to complete the quests is one of the key elements, game designers need to consider. Games that have elements which encourage positive emotions and tense feelings, rather than excitement and continuous challenge are more suited to the elders [17]. Additionally, research shows that it is more beneficial for AD patients to be helped through the completion of a challenge, rather than see the challenge failed [18]. It is important to present both audio and visual cues to cater to the needs of a specific profile of patients suffering from either visual or auditory impairments [13]. Thus, real-time assistance with audio and visual feedback is one of the mandatory components in games for elders, to incorporate mechanism which achieves high-level engagement by keeping player filled with positive emotions.

3 Orientation Game

We created a fully immersive and interactive VR environment that is adaptable in real- time using Unity 3D. We aim to integrates the benefits induced by the creation of a cognitive map of the surroundings in a fully immersive 3D VR environment. Items are placed at a suitable distance from each other throughout the garden, forcing users to explore the environment. The guidance system is designed to help the users in completing the tasks without being overloaded with negative emotions.

3.1 Environment: Orientation Game

We designed a VR environment that simulates a botanical garden. The environment is in the form of 5x5 maze where trees make up the walls of the maze and clearings through the trees are the pathways. The user navigates on the environment using a joystick by clicking in the direction in which they wish to move. The user can see other elements in the game: a map of the garden, their position and direction in the form of a red arrow on the map, a blue circle representing the target location of the items (dis-played when the game starts or when a hint is shown), visual hints and verbal messages displayed when needed.

When the game starts, the user is introduced to a tutorial to familiarize with the environment and the controls. We explain the elements displayed in the game, we provide an example item to find and collect which allows the users to understand the movement within the environment and the different types of hints. Once the tutorial finishes and the user is ready, the game can start. The game consists of four quests. In each of the first three quests, we start by asking the user to collect an item which is in a specific location of the maze. The item's name is displayed in a list and its location is indicated by a flashing circle on the map for 5 second. The user must then reach this location and collect the requested item. Once the user has arrived at the correct location, they must search for it by looking around and click joystick button to collect it. Every time an item is collected, we display the list remove it from the list and show the next item with its location. When all the three items are collected, one at a time, the user is presented to the fourth one. For the last quest, the user needs to return to the starting point and put the three collected items in a basket. The items are lavender, coconuts, and apples. Figure 1 shows the different elements displayed in the environment at the start of the game.

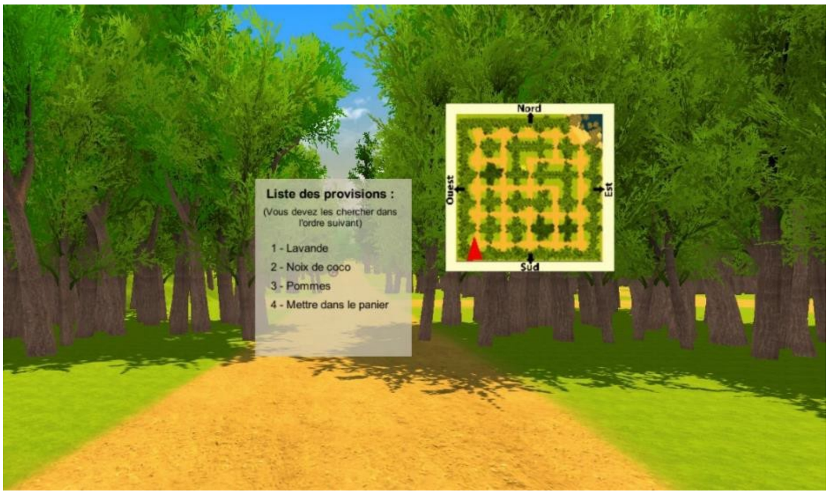

Fig. 1. The list of items to collect and the map representing the environment.

3.2 Guidance System

The guidance system actively tracks participant's emotions and movement and provides hints that help to complete the tasks of the game. The list of emotions used in this experiment are provided by Emotiv proprietary software: frustration, excitement, engagement, meditation, and valence. Although we do not have access to the Emotiv system proprietary algorithms to infer mental states from raw data and frequency bands, several studies have established the reliability of the output. It also keeps track of the history of the participant's movement and actions that are taken while completing the quests within the maze. The guidance system sits outside the VR environment and the emotions tracking system, and it receives emotions of the participants as well as their position every second.
There are three different types of activation of hints:

1. Emotions: At every timestamp, the mean of the change and the rate of the change of emotion values every ten seconds are used to calculate a net score for each emotion. The emotion with the maximum score is compared with an empirically defined threshold. A score higher than the threshold activates the emotion-based hints
2. Away from target: If the participant takes three steps or more, all of which are at four blocks or more from the target, the hint level 2-1 is activated.
3. No Movement: If the participant does not move for more than a given amount of time, the hint 2-1 based on no movement is activated.

Hint levels		Participant's position	Object's location	Message (Audio and Visual)	Highlighted Path in Map
Level 1		✓	✓		
Level 2	2-1	✓	✓	*Please check the position of the object on the map and try to reach it.*	
	2-2	✓	✓	*You are too far. Try to take a few steps back.*	
	2-3	✓	✓	*1. Good job, you're almost there!* *2. Keep up the good work!* *3. You are in the right direction!*	
Level 3		✓		*Follow the path indicated, the object is nearby.*	Path to cell nearest to target object
Level 4		✓		*Follow this path, you will find the object.*	Complete path to the object.

Fig. 2. Different levels of hints

Figure 2 displays the level of detail provided in different hints. The number of details provided by the guidance system increases progressively with the level of hints. Level 1 provides the least information and displays only the participant's location and the object's location on the map. Additionally, level 2 displays a text message in a prompt in the VR environment along with the verbal narration of the message. Level 3 hint highlights a path in the map, which the participant can follow to reach a location immediately next to the actual location of the object. This still leaves some scope of exploration and allows the participant to search for the object in all possible directions. Level 4 hint highlights the complete path leading to the object's location on the map. In case of activation based on participant’s emotion, if the hint is triggered by a negative emotion such as frustration, the level of hint increases which subsequently provides more details to find the object. On the other hand, if the hint is triggered by positive emotions such as excitement or engagement, the level of hint decreases. In case of hint activated due to no movement of the participant, the level increases every fifteen seconds till the participant moves, at which point it resets to level 1. When the participant is away from the object as determined by the guidance system, the hint provided is always level 2-1.

Once the help is received by the VE, the latter displays it as a text/sound message or as a path displayed on the map. The way the help is displayed depends on the hint level described earlier. As an example, figure 3 shows the hint level 4 as a complete path to the target location on the map, where the numbers represent the steps the user must follow to reach the target position. Hint is given with a verbal message asking the user to follow the steps displayed which will lead then to the item. Every hint when dis-played, remains on the screen for a duration of four seconds.

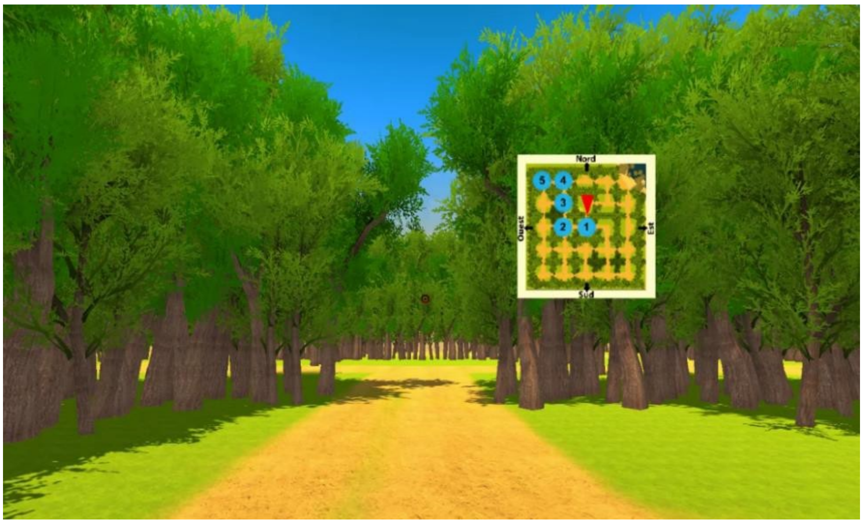

Fig. 3. Hint level 4

4 Experiments

We analyzed the impact of our orientation game on the attention and memory perfor-mance to test the performance of our approach which is based on the cognitive map theory. Therefore, in addition to the game, we developed 3 attention exercises et 3 memory exercises to compare participants’ performances before and after the therapy.

4.1 Attention exercises

The participant starts with the first attention exercise. In this exercise, we present a sound sequence of 5 numbers then a numerical pad is displayed, and the participant must repeat the same sequence; then we hide the pad, we present another sound sequence of 3 numbers and the participant must report the sequence in the backward order. In the second attention exercise, we present a sound sequence of different letters at a rate of one per second and the participant must click the space bar each time they hear the letter “A”. The third attention exercise is about naming different objects. For every object, we show an image for 4 seconds then we replace it by four letters and the participant is asked to select the first letter of the object’s name.

4.2 Memory exercises

The fourth exercise which is the first memory exercise is a contextual memory test. The participant is asked to memorize a series of different objects which are presented either visually or orally with their names. Once the series is over, we introduce a series of objects’ images or names presented auditorily. For each object, the participant must determine whether the object showed or heard was presented in the first series of ob-jects. They must tell if it was seen visually, auditorily or never presented in the previous series by clicking on one of the 3 buttons displayed. For instance, an image of a ship is shown in the first series, and in the second series, the participant should choose if they saw it, heard its name, or if the object was not presented in the previous sequence.

In the fifth exercise, which is a short-term memory test, we start by presenting ten white circles. Then we highlight a series of circles one by one to create a se-quence and the participant is asked to memorize it. The participants are then asked to reproduce the same sequence. We present two sequences with two different levels of difficulty.

The sixth and last memory exercise is a working memory one. We present a set of 3 pictures for a short period of time that the participant must memorize. Then, this set is replaced by four sets of three pictures and the participant is asked to identify the set which was presented. They do this for two sets.

4.3 Process of the experiment

Our approach was performed on 17 participants (13 females) with subjective cognitive decline (SCD). The mean age was 72.76 with a standard deviation SD = 5.66. Each participant must go through two sessions.

In the first session, we described the study to the participants and invited them to sign a consent form. Then, we asked them to perform clinical tests in order to confirm diagnosis and determine whether they are eligible to participate in the experiment or not. Once we make sure that a participant is eligible, they are invited to take part in the experiment. We invite the participant to fill two pre-experiment forms: the Positive and Negative Affect Schedule (PANAS) scale [20], a self-assessment of emotions, and a questionnaire on cyber-sickness [21].

Once they finish the first step, the participant is equipped with an EEG headset and is invited to resolve attention and memory exercises. After the participant finishes the exercises, they are equipped with Fove VR headset and can start the orientation therapy. Participants are encouraged to take the time they need in order to navigate in the environment. Once the orientation therapy game is finished, we remove the Fove VR headset and the participant is invited to complete the same 6 exercises with different examples than the first time.

Finally, we remove the EEG headset and the participant fills up four post-experiment forms: PANAS scale, cyber-sickness, the AttrackDiff 2 [22] and a self-report form. Figure 4 shows the different steps of the process of the experiment.

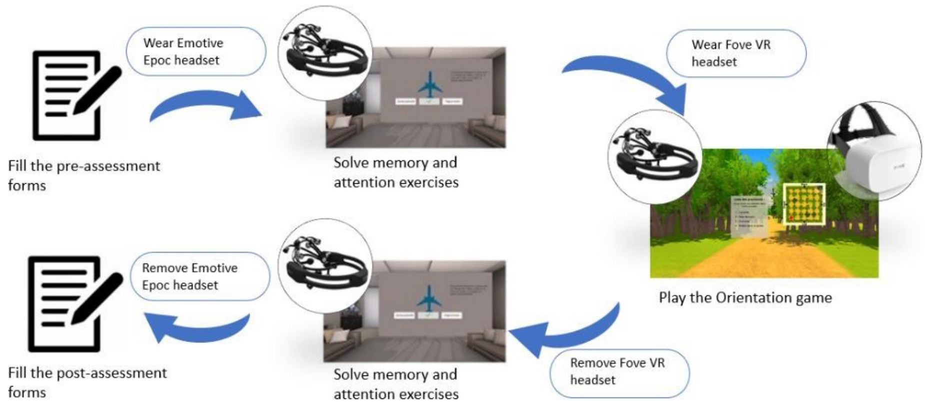

Fig. 4. Process of the experiments

5 Results and Discussion

The first objective of this research is to check whether **it is possible to improve memory and attention performance through a virtual maze game**. We started by analysing the difference between the performance before and after the orientation therapy. For the attention exercises, the performance improvement are as follows: On the exercise 1, the general mean improvement was 4.41%. For exercise 2, the performance improvement was 1.6%. On the third exercise, there was a mean improvement of 0%. We also analysed the improvement of the memory exercises. For exercise 4, the mean improvement was 0.98%. On exercise 5, there was a mean improvement of 12.94%. For exercise 6, the mean frustration was 32.35%. We note that exercise 6 has the highest percentage of improvement. We analysed then the attention exercises versus the memory exercises. Figure 5 shows a clear difference between the improvement of performance on attention exercises versus the memory exercises.

Fig. 5. Histogram of performance improvement for attention vs memory exercises

The trend obtained in our first analysis lead to our second research question which is to check whether it is possible to reduce participants' negative emotions by helping them to orient in the orientation game. To this end, we analyzed the frustration of the participants before and after the hints was given. Figure 6 shows a comparison of mean of the total frustration in ten seconds before the hint was provided and next ten seconds after the hint was provided.

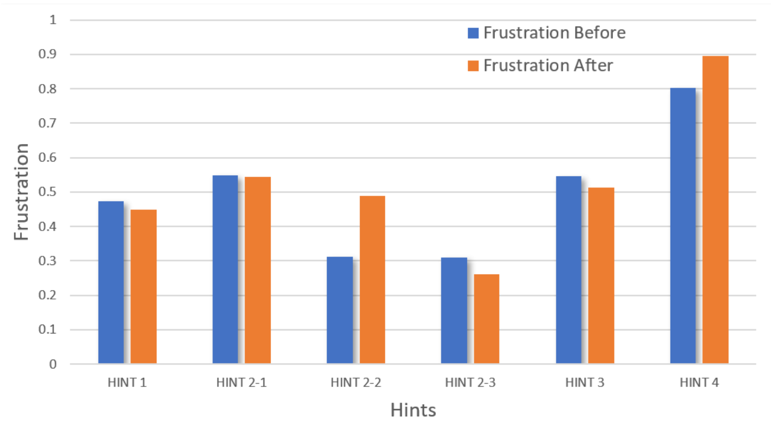

Fig. 6. Average values of frustrations for each hint over all the participants, 10 seconds before and after the hints were provided.

For the different types of hints, we observed that except for hint level 2-2 and hint level 4, the average values of frustration for all the participants were lesser in the next ten seconds after the hints were provided. Hint level 2-2 provides a warning message: 'You're too far. Try to take few steps back.'. This led the participants to believe that they might be doing something wrong leading to higher frustration. Hint level 4 displays the complete path to the item's location. But, since we configured the hint to appear for only four seconds, it was not enough for the participants to memorize the complete path to the item's location, which may have led to a higher level of frustration.

In the after-experiment survey, 78% of the participants found the hints to be helpful to solve the quests, which further supports the utility of the real-time guidance system in 3D VR orientation games.

6 Conclusion

In this paper, we presented a novel approach to intelligently help patients suffering from pre-clinical states of Alzheimer's disease to orient in a fully immersive virtual reality maze game to improve their attention and memory performance. We conducted experiments involving 17 participants and results show that after the orientation game, almost all participants had an improvement in memory performance. Results show that the real-time guidance system is helpful to the participants in completing the tasks in the game. Simple and positive hints help to stabilize the frustration of participant and complete the given tasks. However, hints which have a warning tone or are more difficult to understand may have opposite effect and increases their frustration. This shows that audio-visual hints in a serious game for elderly should have positive message and be easy to comprehend.

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