

Application of Virtual Travel for Alzheimer's Disease

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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 Abdesslem 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 β A 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".

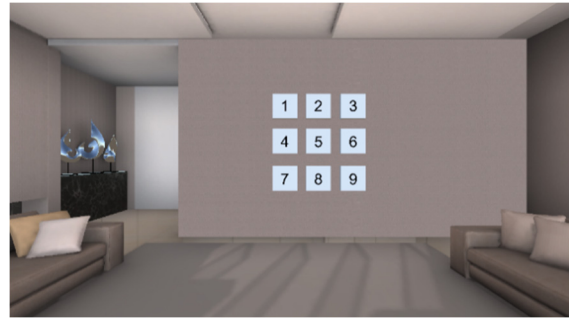


Figure 3: Screen capture of exercise 1.

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.

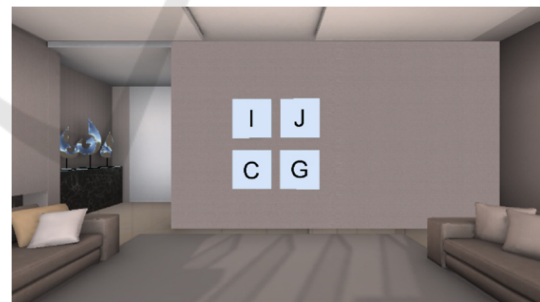


Figure 5: Screen capture of exercise 3.

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.

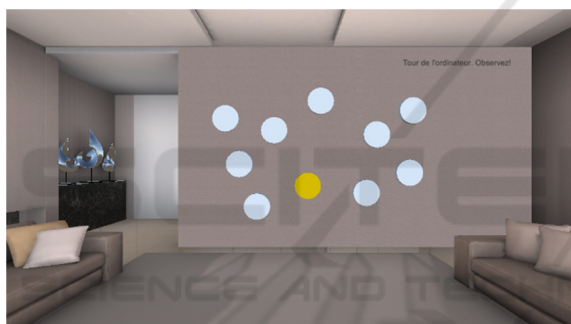


Figure 7: Screen capture of exercise 5.

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.

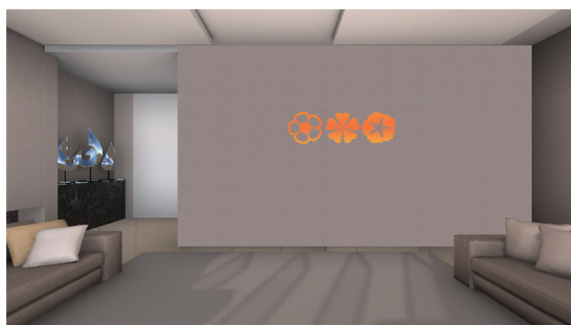


Figure 8: Exercise 6: Set to be memorized.

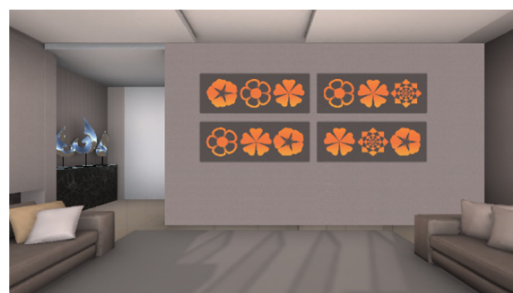


Figure 9: Exercise 6: Four sets from which the correct set should be identified.

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 (Lallemant 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.

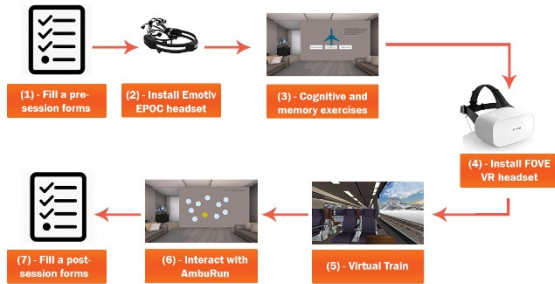


Figure 10: Process of the experiment.

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.

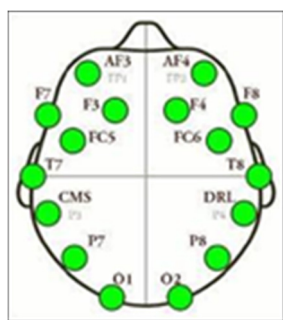


Figure 11: Emotiv headset sensors placement.

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.

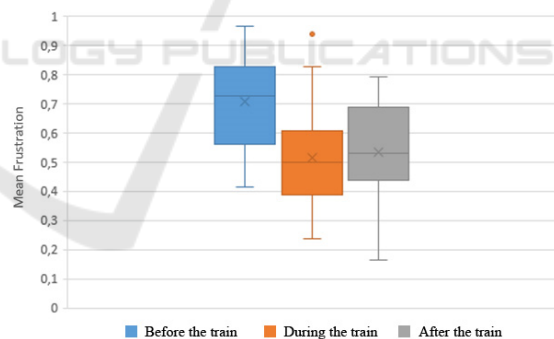


Figure 12: Boxplot of general mean frustration.

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.

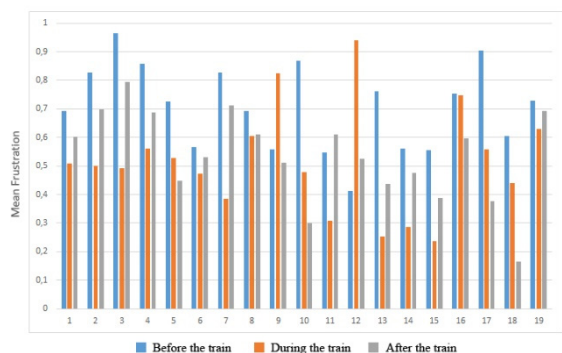


Figure 13: Histogram of mean frustration in individual participants.

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.

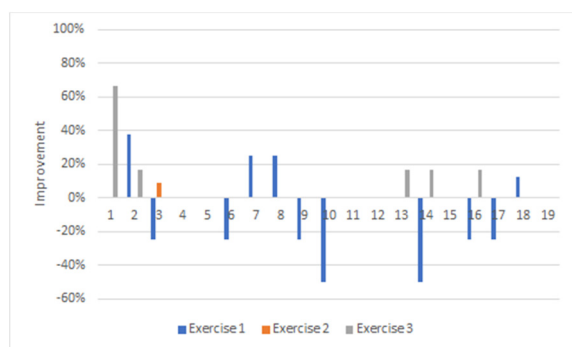


Figure 14: Histogram of performance improvement in exercise 1, 2 and 3.

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.

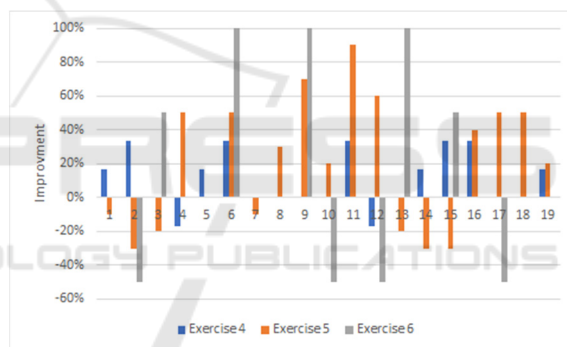


Figure 15: Histogram of performance improvement in exercise 4, 5 and 6.

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.

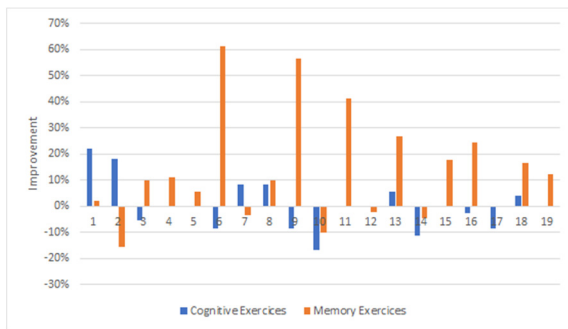


Figure 16: Histogram of performance improvement cognitive vs memory exercises.

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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REFERENCES

- Alvarez, R. P., Johnson, L., & Grillon, C. (2007). Contextual-specificity of short-delay extinction in humans: Renewal of fear-potentiated startle in a virtual environment. *Learning & Memory, 14*(4), 247–253.
- Appel, L. (2017). *How Virtual Reality could Change Alzheimer Care*. Technologie. Retrieved from <https://fr.slideshare.net/TechnoMontreal/how-virtual-reality-could-change-alzheimer-care>
- Aspinall, P., Mavros, P., Coyne, R., & Roe, J. (2015). The urban brain: Analysing outdoor physical activity with mobile EEG. *British Journal of Sports Medicine, 49*(4), 272–276.
- Association, A. (2015). 2015 Alzheimer's disease facts and figures. *Alzheimer's & Dementia, 11*(3), 332–384.
- Ben Abdesslem, H., Chaouachi, M., & Frasson, C. (2019). Toward Real-Time System Adaptation Using Excitement Detection from Eye Tracking. 15th International Conference on Intelligent Tutoring Systems, 214–223.
- Ben Khedher, A., Jraidi, I., & Frasson, C. (2018). What Can Eye Movement Patterns Reveal About Learners' Performance? 14th International Conference on Intelligent Tutoring Systems, 415–417.
- Ben Khedher, A., Jraidi, I., & Frasson, C. (2019, January 18). Tracking Students' Mental Engagement Using EEG Signals during an Interaction with a Virtual Learning Environment. *Journal of Intelligent Learning Systems and Applications*, pp. 720–726.
- Berka, C., Levendowski, D. J., Lumicao, M. N., Yau, A., Davis, G., Zivkovic, V. T., ... Craven, P. L. (2007). EEG correlates of task engagement and mental workload in vigilance, learning, and memory tasks. *Aviation, Space, and Environmental Medicine, 78*(5 Suppl), B231-244.
- Biamonti, A., Gramegna, S., & Imamogullari-Leblanc, B. (2014). A Design Experience for the Enhancement of the Quality of Life for People with Alzheimer's Disease. What's On: Cumulus Spring Conference.
- Bioocca, F. (2006). The Cyborg's Dilemma: Progressive Embodiment in Virtual Environments [1]. *Journal of Computer-Mediated Communication, 3*(2), 0–0.
- Cherniack, E. P. (2011). Not just fun and games: Applications of virtual reality in the identification and

- rehabilitation of cognitive disorders of the elderly. *Disability and Rehabilitation: Assistive Technology*, 6(4), 283–289.
- Cirrito, J. R., Yamada, K. A., Finn, M. B., Sloviter, R. S., Bales, K. R., May, P. C., ... Holtzman, D. M. (2005). Synaptic Activity Regulates Interstitial Fluid Amyloid- β Levels In Vivo. *Neuron*, 48(6), 913–922.
- Coyle, H., Traynor, V., & Solowij, N. (2015). Computerized and Virtual Reality Cognitive Training for Individuals at High Risk of Cognitive Decline: Systematic Review of the Literature. *The American Journal of Geriatric Psychiatry*, 23(4), 335–359.
- Dubois, B., Feldman, H. H., Jacova, C., DeKosky, S. T., Barberger-Gateau, P., Cummings, J., ... Scheltens, P. (2007). Research criteria for the diagnosis of Alzheimer's disease: Revising the NINCDS-ADRDA criteria. *The Lancet Neurology*, 6(8), 734–746.
- Gorini, A., & Riva, G. (2008). Virtual reality in anxiety disorders: The past and the future. *Expert Review of Neurotherapeutics*, 8(2), 215–233.
- Hill, N. T. M., Mowszowski, L., Naismith, S. L., Chadwick, V. L., Valenzuela, M., & Lampit, A. (2016). Computerized Cognitive Training in Older Adults With Mild Cognitive Impairment or Dementia: A Systematic Review and Meta-Analysis. *American Journal of Psychiatry*, 174(4), 329–340.
- Kennedy, R. S., Lane, N. E., Berbaum, K. S., & Lilienthal, M. G. (1993). Simulator Sickness Questionnaire: An Enhanced Method for Quantifying Simulator Sickness. *The International Journal of Aviation Psychology*, 3(3), 203–220.
- Laforge, M. (2018). Zoothérapie: Tout savoir sur la thérapie assistée par les animaux. Retrieved October 23, 2019, from Canal Vie website: <http://www.canalvie.com/famille/animaux/zootherapie-1.1767466>
- Lallemand, C., Koenig, V., Gronier, G., & Martin, R. (2015). Création et validation d'une version française du questionnaire AttrakDiff pour l'évaluation de l'expérience utilisateur des systèmes interactifs. *Revue Européenne de Psychologie Appliquée/European Review of Applied Psychology*, 65(5), 239–252.
- Lawton, M. P., Van Haitsma, K., & Klapper, J. (1996). Observed Affect in Nursing Home Residents with Alzheimer's Disease. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 51B(1), P3–P14.
- Manera, V., Chapoulie, E., Bourgeois, J., Guerchouche, R., David, R., Ondrej, J., ... Robert, P. (2016). A Feasibility Study with Image-Based Rendered Virtual Reality in Patients with Mild Cognitive Impairment and Dementia. *PLOS ONE*, 11(3), e0151487.
- Maynard, O. M., Munafò, M. R., & Leonards, U. (2013). Visual attention to health warnings on plain tobacco packaging in adolescent smokers and non-smokers. *Addiction (Abingdon, England)*, 108(2), 413–419.
- Pedraza-Hueso, M., Martín-Calzón, S., Díaz-Pernas, F. J., & Martínez-Zarzuola, M. (2015). Rehabilitation Using Kinect-based Games and Virtual Reality. *Procedia Computer Science*, 75, 161–168.
- Pini, L., Pievani, M., Bocchetta, M., Altomare, D., Bosco, P., Cavado, E., ... Frisoni, G. B. (2016). Brain atrophy in Alzheimer's Disease and aging. *Ageing Research Reviews*, 30, 25–48.
- Robert, P., Lanctôt, K. L., Agüera-Ortiz, L., Aalten, P., Bremond, F., Defrancesco, M., ... Manera, V. (2018). Is it time to revise the diagnostic criteria for apathy in brain disorders? The 2018 international consensus group. *European Psychiatry*, 54, 71–76.
- Rose, F. D., Brooks, Barbara. M., & Rizzo, A. A. (2005). Virtual Reality in Brain Damage Rehabilitation: Review. *CyberPsychology & Behavior*, 8(3), 241–262.
- Todd, R. M., & Anderson, A. K. (2009). The neurogenetics of remembering emotions past. *Proceedings of the National Academy of Sciences*, 106(45), 18881–18882.
- van Dalen, J. W., van Wanrooij, L. L., Moll van Charante, E. P., Brayne, C., van Gool, W. A., & Richard, E. (2018). Association of Apathy With Risk of Incident Dementia: A Systematic Review and Meta-analysis. *JAMA Psychiatry*, 75(10), 1012.
- Vindenes, J., de Gortari, A. O., & Wasson, B. (2018). Mnemosyne: Adapting the Method of Loci to Immersive Virtual Reality. In L. T. De Paolis & P. Bourdot (Eds.), *Augmented Reality, Virtual Reality, and Computer Graphics (Vol. 10850, pp. 205–213)*.
- Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, 54(6), 1063–1070.
- Zhu, C. W., Grossman, H. T., & Sano, M. (2019). Why Do They Just Sit? Apathy as a Core Symptom of Alzheimer Disease. *The American Journal of Geriatric Psychiatry*, 27(4), 395–405.
- Zucchella, C., Bartolo, M., Bernini, S., Picascia, M., & Sinforiani, E. (2015). Quality of Life in Alzheimer Disease: A Comparison of Patients' and Caregivers' Points of View. *Alzheimer Disease & Associated Disorders*, 29(1), 50–54.