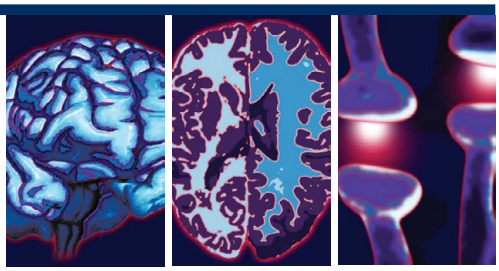

Impact on Information and Communication Technologies versus anaerobic physical activity in patients with mild Alzheimer´s disease: A pilot study

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ABSTRACT

Objectives:

Evaluate the impact of information and communications technology (ICT) versus anaerobic physical activity in patients with mild Alzheimer´s disease on level of stress, anxiety and depression.

Method:

The design is an quasi-experimental and prospective study. It applies both types of non-pharmacological therapies to 24 patients with mild Alzheimer's disease (12 for each therapy) for 4 weeks (twice a week). Before and after each session, salivary cortisol samples, quantified by ELISA, were collected, and Hospital Anxiety and Depression Scale (HADS) questionnaires were used.

Results:

For both therapies, the results show a significant improvement in the perception of anxiety and depression through HADS questionnaires. While stress level (measured by quantification of cortisol in saliva) improved non-significantly after exercise based on ICTs, it increased with anaerobic exercise.

Discussion:

Both therapies decreased the perception of anxiety and depression, supporting the suggestions reflected in other studies. Nevertheless, anaerobic exercise increased physiological stress as opposed to aerobic exercise, according to other authors. ICT based exercise decreased it, becoming a more suitable therapy for these patients.

Keywords

Alzheimer, Cortisol, Physical Exercise, Depression, Anxiety, TICs, Dementia

Introduction

Alzheimer's disease (AD) is defined as a neurodegenerative disorder with an estimated survival rate of 3 to 9 years [1] which presents degenerative and pathological symptoms, as well as a progressive decline of the cognitive state, such as language, memory, executive function and social deterioration [2]. Its appearance and

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development is associated with depression and anxiety [3].

The maintained emotional stress is associated to the AD as a consequence of neuronal death, mainly due to the accumulation of beta-amyloid peptide and tau protein [4,5]. Different studies show evidence that high level of chronic stress causes depression basically because of monoaminergic changes that are generated in various brain regions and the suppression of hippocampal neurogenesis [6]. This neuronal degeneration could also affect the limbic structures associated with emotional regulation, which explains the appearance of anxiety in many patients [7].

Stress activates a specific neuroendocrine pathway, the hypothalamic-pituitary-adrenal axis (HPA) [8]. The stimuli, perceived as stressful, activate the hypothalamus through the corticotropin-releasing factor (CRF) and stimulates the release of the adrenocorticotropic hormone (ACTH) in the pituitary gland, which in turn acts on the adrenal cortex producing glucocorticoid hormones, primarily cortisol, considered to be the most reliable biomarker for measuring physiological stress levels in any biological sample [9,10]. Cortisol is quantified in blood, saliva, sediments and hair mainly. Among these, salivary cortisol is used as a biomarker of psychological stress. Nevertheless, this measurement can be affected by the sources of variance. For example, the influence of variables such as estrogens, gender, menstrual cycle or oral contraceptives could affect cortisol binding [11]. However, this type of measurement is a faster and non-invasive method for the patient, which has become popular [12] and precisely, in these Alzheimer's patients (women over 65 years) the effects of menstrual cycle or oral contraceptives are not present. Nowadays, AD has no cure and pharmacological treatment only alleviates the symptoms. For this reason, the role of non-pharmacological therapies (NFTs) is important, which are very diverse and are based on brain plasticity [13], delaying functional deterioration and disability in Alzheimer patients [14].

In this context, aerobic exercise reduces the risk of dementia, AD and cognitive impairment [15,16], besides reducing the risk of suffering from psychological and emotional disorders such as anxiety and depression [17]. In the case of very evident disease, physical exercise offers promising results as a dementia complementary treatment, slowing down the process of skill loss [18]. New technologies are becoming more popular in the field of physical exercise due to the information and communications technologies (ICTs), based on the use of software on computers, game consoles, tablets, smart phones, etc. with the aim of training or stimulating cognition and memory [19].

The aim of the study was to compare the influence of anaerobic exercise and ICTs-based physical activity, related to stress and the perception of anxiety and depression in patients with mild Alzheimer's.

Methods

■ Study design

It is a quasi-experimental and prospective study.

■ Participants

The participants of this study are Alzheimer's patients from a Valencia association called *AFAV*. The inclusion criteria were men and women older than 60 years with mild Alzheimer's disease. To determine the diagnoses of Alzheimer's disease (AD) the same score ranging from 18 to 23 was used for all the patients in the Mini Mental State Examination (MMSE). These tests were performed by the professional neuropsychologist of the center. The MMSE is a commonly used method to study cognitive impairment and to assess the outcome of patients with these symptoms through different questions and tasks that the patients are asked. The evaluation system consists in increasing the punctuation when the patient responds correctly, allowing us to assess different aspects like orientation, attention, concentration, memory or language [20,21].

We excluded the patients who refused NFT or who had psychiatric disorders which interfered in their capacity to understand basic instructions, or which caused behavioral problems. The final sample was 24 patients divided randomly in two groups of 12 patients each, one group in the Study 1 and other in the Study 2.

In Study 1, which assessed anaerobic physical exercise, average age was 75.21, with a standard deviation of ± 7.45, being 85 the maximum age and 62 the minimum, where 50% were women and 50% men. However, in Study 2, which assessed ICTs-based physical activity, the participants' average age was 72.83 years old, with a standard deviation of ± 8.09, being the

maximum age 82 and the minimum 62, where 50% were male and 50% female.

It is known that 1.00 - 3.33 ηg/ml is the value of cortisol reference interval in adults without AD at 12 p.m (Venero et al., 2013) and the standard values of people without AD in anxiety/depression perception measured through HADS test are 0-7 points [22].

Since this is a pilot study we are presenting the standard values of cortisol, anxiety and depression in patients without AD. No control group has been used. It is not relevant because the main objective of the study is to observe the differences between both therapies in AD patients. Moreover, comparing the two therapies at the same time of day and the same day of the week eliminates the differences caused by the circadian rhythm.

Procedure

The therapies were performed during 4 weeks, two days a week (Monday and Thursday) and at the same time (10 a.m.). Before and after the sessions, a sample of saliva from the participants was obtained (1.5 ml) and a HADS test was performed **(Table 1)**. Both therapies (ICTs *vs* physical activity) were performed at the same time in both groups to reduce the strange variables in the results.

The test results were recorded in a data base for posterior statistical analysis. Using the saliva sample, the cortisol concentration was quantified by means of the immunoassay technique, processing the results obtained. Salivary cortisol samples were obtained by a specialist nurse in this area.

Instruments

The anaerobic exercises were carried out with foam and medicine balls. This first therapy consisted in simple exercises, all of them supervised by the physiotherapist of the center to determine the length, intensity, rhythm and structure of these activities. Examples of these physical activities are passing the ball with hands, sitting down and getting up with the ball in their hand or passing the ball with the flexed legs. Prior to these physical activities the patients did training phase with the objective to reduce injuries.

On the other hand, therapy based on ICTs consisted in the use of consoles (concretely X-BOX 360 with Kinect Microsoft device and Kinectimals play).

Table 1: Distribution of therapies, interviews and saliva sample collections.

	N	Day of week	Time	Duration	9:45H	10:45H
Study 1	12	Monday Thursday	10 a.m.	45 min	Saliva collection HADS	Saliva collection HADS
Study 2	12	Monday Thursday	10 a.m.	45 min	Saliva collection HADS	Saliva collection HADS

The patient played a rings game, 15 minute each (total of 45 minutes), which is a free game and training controller that enables users to control and interact with the console through a natural user interface that recognizes gestures, voice commands, objects and images. The game was about covering holes in the ground with the hands, feet and body through movements for 45 minutes. The intensity and duration of this computer games were determined by the psychologist of the center too.

Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) test, which consists of 14 items (the higher score indicating less depression and anxiety), divided into two subscales with 7 items, which assessed depression or anxiety [23]. The scale has high internal consistency (alpha Cronbach of 0.7-0.9) and high stability (r>0.80) [23]. The HADS test, despite being a self-report scale which is very simple, with few questions, and only for patients who are still aware of their emotions, is considered appropriate for this study.

We measured cortisol in the 24 samples by a solid-phase, competitive chemiluminescent enzyme immunoassay (Immulite, Siemens), displaying within-run and between-run imprecision lower than 10%, recovery rates between 92% and 120%, and a limit of detection of 0.2 nmol/L [24]. ELISA tests were carried out as per manufacturer's instructions (Salivary Cortisol ELISA SLV-2930 kit, DRG International Inc.)

Data analysis

Non-parametric Mann-Whitney-Wilcoxon Statistical test was applied due to the quality of the study.

Ethical considerations

In this study, ethical issues were taken into account. We considered all the basic principles of the biomedical research, described in the Declaration of Helsinki [25], with the approval of the research ethics committee of the Commission on Human Ethics in Experimental research of the University of Valencia on June 29, 2015.

Table 2: Differences in anxiety, depression and cortisol after physical exercise with ICTs and anaerobic physical exercise.

	ANXIETY				DEPRESSION				CORTISOL (ηg/ml)			
	BEFORE		AFTER		BEFORE		AFTER		BEFORE	AFTER		
	EXER	ICTs	EXER	ICTs	EXER	ICTs	EXER	ICTs	EXER	ICTs	EXER	ICTs
Average	4.25*	2*	2.67*	.83*	6.4*	3.25*	2.76*	1.33*	7.79	6.48	8.22	6.01
T. D.	3.05	1.21	2.06	1.11	5.51	.75	3.05	.49	2.86	2.55	1.24	3.74

Signification levels: *p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001

Results

The results obtained **(Table 2)** show that the perception of anxiety and depression decreases significantly in Study 1 with anaerobic physical exercise and in Study 2 with the application of exercise based on ICTs. In Study 1, there is an increase (non-significant) in the level of cortisol. However, in Study 2, there is a decrease (non-significant).

Discussion

As a consequence of stress, linked to psychiatric disorders such as agitation and anxiety, cortisol level increases in our organism and it induces damage in the brain [26]. This fact particularly remarkable in neurodegenerative disorders like Alzheimer's. Nowadays, this illness does not have any cure, hence NFT are interesting to improve treatment and stop the progress of this disorder. Physical exercise improves anxiety on patients with chronic diseases, more precisely, in AD patients, decreases neuropsychiatric symptoms [21]. The results obtained in our study support this because the anaerobic physical exercise improves significantly the anxiety and depression perception.

Exercise with ITCs also improves significantly both variables. These results confirm the positive effect of ICTs in patients with dementia who have therapies based on new technologies associated to other cognitive stimulation therapies [14,27].

However, there are discrepancies between the influence of the exercise and the variation of cortisol levels in patients with dementia. It has been shown that aerobic exercise decreases cortisol levels in blood in patients with lactose intolerance at risk of dementia [28,29]. On the other hand, in patients with mild cognitive deterioration, this influence above mentioned depends on the gender, because cortisol decreases in women and increases in men [28,29]. Our study, with 50% of men and 50% of women, shows that anaerobic physical exercise increases cortisol in saliva (but not significantly) and aerobic exercise based on ICTs decreases it. This result may be explained by the stress levels associated with the type of exercise, because the emotional component is very relevant on ICTs and it can decrease the level of cortisol. Maybe for AD patients exercise using video games is more positive and less stressful than anaerobic exercise, and this would explain our results.

Due to this finding, we consider that future research with larger samples in this area is needed to confirm the tendency observed on three parameters measured (perception of anxiety, depression and stress levels), so it can be used as a predictor. Despite the results obtained, our study has limitations, such as the small sample size, attributable to reluctance to participation from some patients or their legal representatives. On the other hand, further studies with more methodological rigor are necessary to confirm the results obtained in this study, where optimal size sample or confidence interval was studied. Moreover, other limitation of this study is based on the influence of hormonal states in the female patients and we have not measured estrogen concentrations. However, we have worked with patients older than 65, and these effects are more much reduced. Further studies are therefore needed in this field, involving larger patient samples. It is only a pilot study [30-33].

Conclusion

Despite of the limitations of our pilot study, physical exercise based on ICTs seems to be an effective therapy to improve anxiety and depression perception and seems to decrease cortisol level in patients with mild Alzheimer's. Maybe, it can be a good treatment option for this disease. Although more studies in this line are absolutely necessary to confirm these results, the use of ICTs in AD patients can be a new research field. On the other hand, anaerobic physical exercise could increase the level of physiological stress on patients with mild Alzheimer's, despite improving emotional perception.

Conflict of interest statement

No conflict of interest has been declared by the author(s).

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