Supporting Physical and Cognitive Training for Preventing the Occurrence of Dementia Using an Integrated System: A Pilot Study

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Abstract. The project proposes a comprehensive preventive program of dementia in elderlies with minor cognitive disorders due to neurodegenerative diseases. The program combines physical and cognitive training, by means of an integrated technological system composed of a Virtual Environment, simulating daily activities, a smart garment measuring physiological parameters, a bicycle ergometer and tailoring the system to the specific patient's status. Preliminary results confirm the feasibility of this intervention and appear promising in order to contrast age-related cognitive neurodegeneration.

Keywords: Physical and cognitive training · MCI · Oxidative stress · Virtual environment · Smart garment

1 Introduction

Age-related cognitive changes may progress from mild cognitive impairment (MCI) to dementia, a condition in which memory, behavior and cognition are impaired due to neurodegeneration in the brain. Different neurodegenerative disorders causing dementias are observed in elderly but Alzheimer's disease (AD) is the most frequent accounting for 60–70% of all the forms. The pathological process of AD precedes of decades the clinical severe manifestations of dementia, suggesting the possibility of early interventions in asymptomatic or early mild symptomatic individuals. Among many possible procedures, exercise training and cognitive stimulation have demonstrated some preventive efficacy. Cross-sectional studies in humans suggest that more active individuals may have reduced risk of impairment and dementia [1]. Furthermore, improvements in cognitive function in older subjects have also been reported from supervised aerobic training interventions [1]. On the other side, it has been recently reported that even

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simple computer-based virtual environments were effective in enhancing cognition of older adults [2].

Patients with AD and even individuals with MCI [3], often exhibit disorders in Visuospatial (VSP) abilities, such as difficulties with reading, discriminating forms and colors or perceive contrasts, failures to identify objects (agnosia) or to locate them into the environment, deficits of spatial orientation and motion detection, difficulties in developing visual strategies (i.e. to avoid obstacles, point to or grasp objects). Individuals with MCI show preserved brain plasticity and indication exists that cognitive rehabilitation can be a potential efficient method to enhance their cognitive and functional abilities.

Starting from these considerations, this project (GOJI) aimed to develop a comprehensive preventive program tailored on the individual and group characteristics of the cohort (elderly people with minor cognitive disorders) based on the use of a virtual environment and a smart garment, with the purpose of providing an effective and easy accessible technological tool for physical and cognitive stimulation.

2 The Physical and Cognitive Training System

The training system is composed of two main subsystems: a virtual environment simulating daily activities and a smart garment which controls the physiological parameters and regulates the physical exercise intensity properly in order to maintain patient's heart rate at the chosen value.

2.1 Virtual Environment for Supporting Physical and Cognitive Training

The designed virtual environment is composed of two main scenarios, which replicate daily activities: cycling in the park/city and shopping at market.

Both the virtual cycling environment as well as the virtual market one are composed of two steps. The user has to cycle in a park first (purely physical activity) and then in a city, taking care of approaching cars before crossing the streets (jointly physical and cognitive activities). Once in the market, two different tasks, structured according to five different difficulty levels, have to be performed (purely cognitive activity).

Fig. 1. Screenshots of the virtual cycling scenario

The street scenario, in which the user has to cycle on a cycle-ergometer, is designed according to a subjective point of view. During the route for reaching the market the user has to cross some roads stopping and checking that both sides are clear of traffic before proceeding through the intersection. The user uses a joystick for looking at both sides of the road (Fig. 1).

In the market scenario, the user is provided with a shopping-list and has to select accordingly first the appropriate lane containing the products to be purchased as in a real supermarket. Then he/she is asked to detect and select the correct product from the shelf. The number of products in the list, the number of lanes, the amount of items on the shelf and also the position of the target item increase according to the difficulty level selected. Automatic helps (verbal/visive indications) are provided to users if errors occur (Fig. 2).

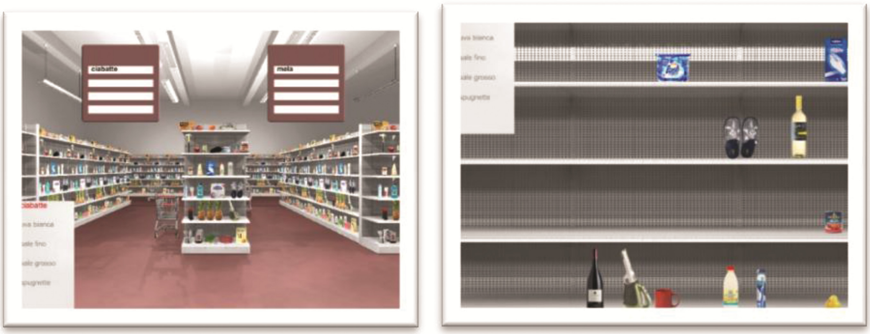

Fig. 2. Screenshots of the virtual market: lane and shelf

Both the street and market scenarios are built in Unity 3D. A cycle-ergometer is integrated into the system (see next paragraph) and a touch-enabled interactive projector is used. The system is thus able to track the gesture of the users and to reveal the point and click activities performed in order to select the proper lane and the requested products on the shelf [4].

2.2 Smart Garment for Heart Rate Monitoring in Virtual Environment Navigation

The navigation of the Virtual Environment for the physical training is carried out by means of a cycle-ergometer (Fig. 3a) and a smart garment (Wearable Wellness System - WWS) (Fig. 3b). The WWS integrates an electronic device for the acquisition, the storage and the wireless transmission of the data. The WWS is designed to be suitable and comfortable, reducing the well-known usability problems of the wearable devices. It integrates two textile electrodes and one textile piezoresistive sensor placed in a pocket at the chest level. It has been designed to monitor continuously the most important vital parameters (as ECG, heart rate and breathe rate) and the movements of the end-user (according to the data of the tri-axial MEMS accelerometer integrated inside). The WWS can operate in streaming mode via Bluetooth up to 20 m in free space or in off-line mode, storing the data on the onboard micro-SD card. Data acquired are sampled with different rates (breath-rate@25 Hz, heart-rate@0.2 Hz, 1-derived ECG channel@250 Hz) and transmitted to the PC on which the Virtual Environment is running.

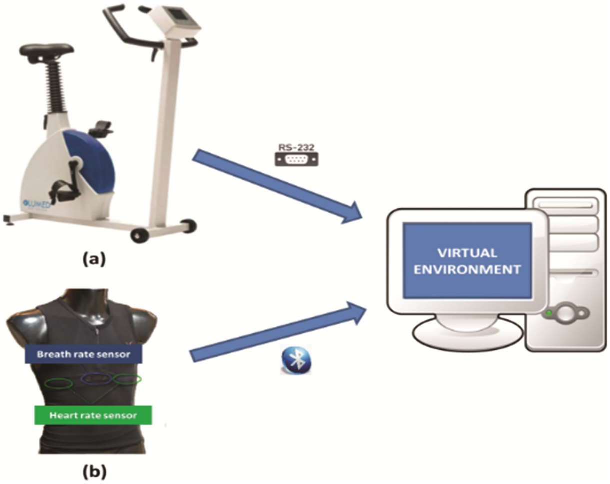

Fig. 3. Overall architecture for fatigue level control at constant HR: (a) the bicycle ergometer used for navigation of VE and (b) the Wearable Wellness System (WWS) used for HR monitoring during the training exercise

An ad-hoc software library manages the user's interaction with the Virtual Environment, integrating functionalities for (a) heart-rate acquisition by the smart garment (via Bluetooth protocol), (b) cycle-ergometer speed acquisition (via RS232 protocol) and (c) setting of the workload of the cycle-ergometer (via RS232 protocol) according to both the cycling speed and the required level of fatigue as defined by the physicians.

The aim of keeping constant the level of effort during training exercise has been reached through the design and the implementation of a digital controller based on a proportional-integral (PI) feedback mechanism.

The control strategy used is inspired from the work of Kawada et al. [5]. In particular, the controller measures the HR provided by the smart garment, compares it with a priori defined HR (heart rate) preset value (about 65% of maximal HR of the subject) and adjusts the workload in order to minimize the difference between them. The difference value is scaled and integrated from the terms of control K_p (proportional gain) and K_i (integral gain). To obtain the correct setting for K_p and K_i a simulation of the overall system was carried out thanks to Simulink Matlab®. The simulation assumes that the controller must stabilize the HR value within specific time constraints. In this work a constraint is that the achievement of the preset HR should be obtained within 3–4 min from the start of the training exercise. From the results obtained, the system is stable in the desired time using the following coefficient: Kp = 0.5, and Ki = 0.04.

3 Description of the Pilot Study

3.1 Experimental Session

This pilot study was performed as a randomized, controlled trial: 10 participants with minor cognitive impairment or mild AD, aged 71 ± 6 years, with 7.6 ± 4.4 years of schooling, were randomly assigned to the experimental group (n = 5), subjected to 3 sessions per week for 6 weeks of Physical and Cognitive Training (Street and Market) for a total of 18 sessions or to a control group (n = 5) that did not receive any kind of stimulation. The duration of training was approximately 40–45 min: 15-20 min of free cycling, about 5 min to perform 5 crossroad passing and 20 min of shopping at the supermarket). The traffic at each intersection (i.e. number and speed of the cars transiting on the road to cross) was determined randomly.

During each session of "shopping" the subject was required to purchase 5 common grocery items. The number of items correctly selected and the number of latencies/omissions/mis-identifications was recorded. The task is designed with increasing levels of difficulty, characterized by the progressive increase of the number of distractors and of their similarity to the target, i.e. of the characteristics to be considered to recognize the correct item among other products. The subject could move to the next level of difficulty after the proper purchase (1 error at the most) of the articles in two consecutive shopping sessions. From the sixth level, the shopping list is hidden, to stimulate memory.

3.2 Assessment of Cognitive Response

In order to verify the positive effects of the training benefits on cognitive and functional capabilities, before the experimental phase (t0), and at the end of the 6 weeks of training (t1), both the experimental and the control group underwent a full neuropsychological assessment. Mini Mental State Examination (MMSE), Rey Auditory Verbal Learning Test (RAVLT), Frontal Assesment Battery (FAB), Rey-Osterrieth Complex Figure Test (ROCFT), Verbal Fluency (VF), Trail Making Test A and B (TMT-a, TMT-b) and Attentive Matrices (AM) were administered for cognitive evaluation. The Functional Activities Questionnaire (FAQ) was used to assess activities of daily living.

These scales tests return numeric values, which can be considered continuous and allow for the comparison of means. For this first pilot phase, t-tests were conducted to compare the scale scores at t0 and t1 within each group, and the changes in scores between t0 and t1 between experimental and control groups.

3.3 Assessment of Physiological Response

Oxidative stress plays an essential role in the pathogenesis of neurodegenerative diseases as it has been suggested that damage caused by Reactive Oxygen Species (ROS) may result in neuronal cell death. Electron Paramagnetic Resonance (EPR) may evaluate oxidative stress measuring the ROS production. Micro-invasive analytic technique for detection ROS concentration by EPR is now demonstrated suitable to monitor physiological and pathological conditions [6].

The physiological impact of training has been evaluated by the assessment of the heart rate profile, the average work rate and ROS production in both the experimental and control groups at t0 and t1.

4 Results and Discussion

4.1 Assessment of Cognitive Response

Participants had a mild cognitive impairment (MMSE = 23 ± 3.4) and a mild functional impairment (FAQ = 9.7 ± 7.3), of borderline significance. In each group we included three subjects with Mild cognitive impairment (i.e. cognitive impairment in the absence of significant impairment of autonomy) and two patients with mild dementia, (i.e. a mild cognitive impairment and a mild/moderate impairment of instrumental skills of daily living). During the trial, two male participants (one belonging to the experimental group and one to the controls) dropped, both due to hospitalization for reasons unrelated to their cognitive impairment.

In Fig. 4, the mean changes in the corrected test scores between t1 and t0 of experimental and control group are shown. The experimental subjects showed a slight improvement in the MMSE, in visual-constructive test and visuospatial tests of attention, while the controls worsened. The experimental group had a greater improvement than controls in the executive test, memory functions and verbal fluency, while showed a greater worsening of Activities of Daily Living (ADL). None of the comparisons within and between groups reached statistical significance at t-tests, reasonably due to small sample, which amplifies the effect of the slight heterogeneity in scores between subjects.

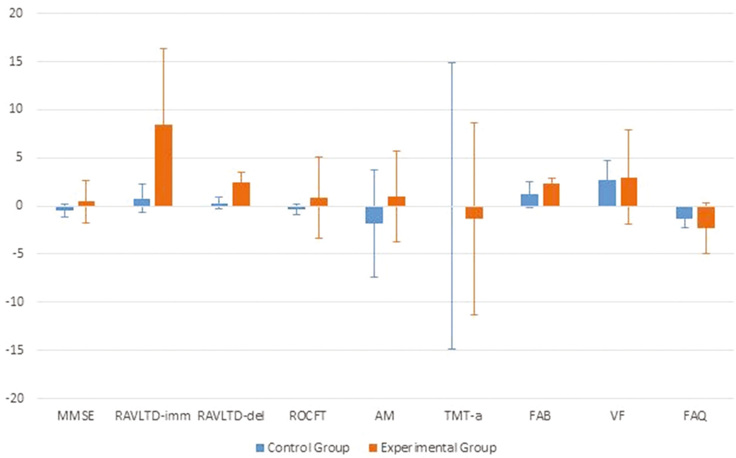

Fig. 4. Mean change scores between the baseline and the end of experimental phase (calculated as t1–t0 scores, except for TMT tests and FAQ implying decreasing scores in relation to better performance, and for which the changes were calculated as t0–t1).

4.2 Assessment of Physiological Response

The compliance to the training regimen was evaluated as "high" (96% of all training sessions were completed as scheduled). Comparing the average work rate performed during the first and the last training sessions a slightly increase was observed whereas heart rate was kept constant.

Compared to the control subjects, in the experimental group after training intervention ROS production rate resulted statistically ($p < 0.05$) lower (2.58 ± 0.32 vs 2.03 ± 0.23 μmol · min^{-1} respectively) (Fig. 5).

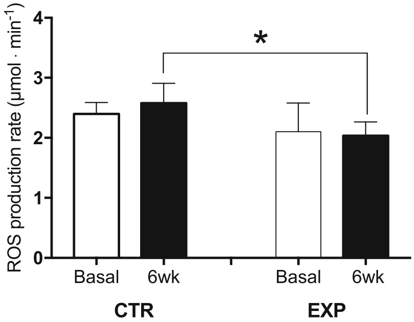

Fig. 5. Histogram plot (mean ± SD) of the absolute ROS production rate (μmol · min^{-1}) obtained from capillary blood in the control (CTR) and experimental (EXP) groups before and after 6 weeks.

After 6 weeks, ROS productions tend to increase with respect to basal value in the control group (2.39 ± 0.18 vs 2.58 ± 0.32 μmol · min^{-1}) and tend to decrease in the experimental group (2.10 ± 0.48 vs 2.03 ± 0.23 μmol · min^{-1}).

This evidence supports the hypothesis that the use of the training protocol may help to delay neurodegenerative damage caused by oxidative stress.

5 Conclusions

The preliminary results of this pilot suggest that the proposed preventive program should be a feasible and effective tool for physical and cognitive stimulation. Further studies, involving more participants, are needed in order to confirm these findings in a larger population.

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