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Acute response of prefrontal cortex in institutionalized older adults undergoing a single exergames session

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ABSTRACT

Virtual reality-based exercise (exergames) improves cognition of the elderly but the neurophysiological effects are poorly understood. The hypothesis herein established is that an ultrafast neurophysiological adaptation occurs in prefrontal cortex of elderly after completion of a single exergames session. To reinforce the aforementioned hypothesis, individuals living in a Long-Term Care Home (LTCH) participated in the study and were randomly allocated into two groups (Virtual Reality Group, VRG, n = 5; and Active Control Group, ACG n = 5). VRG performed six exercises with exergames and ACG performed exercises with the same VRG movements but with no virtual reality. Assessment of frontal cortical activity at rest and during cognitive testing via electroencephalographic activity (EEG) was performed before and immediately after the intervention. Significant decrease in relative power of EEG (RP_{EEG}) Beta brainwave (−29 ± 18%) in the left prefrontal cortex of VRG compared to ACG (4 ± 9%) ($p = 0.007$). A slight improvement on semantic fluency in VRG (ES=0.21) was noted. An ultrafast prefrontal cortical adaptation may occur as an effect of a single exergames session, causing a small improvement on cognition of institutionalized elderly.

1. Introduction

Currently, there is a great interest in the potential of "exergames" as a modality of exercise for the older persons (Laufer et al., 2014). Exergames or virtual reality-based devices, such as the Nintendo Wii and the X Box Kinect, are used by the individual interacting with virtual reality environment. These exercises were developed and designed to stimulate the performance of physical activity while providing an enjoyable experience (Pichierri et al., 2012). Studies have shown the efficacy of exergames on mobility, balance and cognitive functions in older persons (Monteiro-Junior et al., 2016, 2017a, 2017b), with the added advantage of being a low-cost intervention (Stanmore et al., 2017). In addition, people engaged in this type of exercise have reported the intention to change their behavior by continuing to use exergames to improve cognitive and physical functions (Chen et al., 2018). As we showed previously (Monteiro-Junior et al., 2017a, 2017b) exergames can improve cognition and physical capabilities of institutionalized older adults to a greater extent than exercise without cognitive stimulation.

Despite the growth of the use of this technology as a form of exercise for older persons, and clear cognitive, physical, and psychological benefits, neurophysiological effects of this exercise modality have been scarcely explored so far. Neuropsychological modifications have been found acutely and chronically (Monteiro-Junior et al., 2017a, 2017b). In a long-term exposition to exergames, older adults diminished the

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relative power of theta wave in the prefrontal cortex, in line with an improvement in executive function (Schättin et al., 2016). However, it is unclear how the brain of older persons works in a short-term exposition (e.g. a single session) to exergames. To address this matter, two questions arise: 1) A single session of exergames modifies the electrical pattern in the older persons' brain? 2) Could the acute cognitive improvement be explained by an ultrafast neurophysiological adaptation in the older persons' prefrontal cortex?

An easy low-cost method to investigate the superficial electrical activity in the brain is the electroencephalography (EEG), which displays different waves regarding the electrical potential (delta: 1.5–3.5 Hz, theta: 3.5–7.5 Hz, alpha: 7.5–12.5 Hz, beta: 12.5–25 Hz, gamma: >25 Hz) (Rogers et al., 2016). Aging can alter electrical neurotransmission in the brain, potentially resulting in several negative outcomes, such as cognitive dysfunction (Bourisly and Shuaib, 2018). For example, diminished beta power is commonly seen in the frontal cortex of older persons during rest, which could be related to cognitive and behavioral dysfunction (Holschneider and Leuchter, 1995; Koyama et al., 1997). Exergames have been shown to improve cognition in older persons (Monteiro-Junior et al., 2016, 2017a, 2017b) but their effects on electrical mechanisms in the brain are still unclear. Hence, EEG analyses could be helpful to understand how the brain works under cognitive demand, and how different exercise interventions could affect the neurophysiological mechanisms in the older persons' brain in response to exergames.

The aim of this study was to analyze the prefrontal cortical activity and cognitive performance in institutionalized older adults before and immediately after one virtual reality-based exercise session ("exergames").

2. Method

A preliminary randomized, controlled, single-blind trial was conducted. Sample was comprised of 10 older individuals (males and females), aged over 60 years with no dementia, living in a long-term care home from Montes Claros (Minas Gerais, Brazil). Participants were randomized by an independent researcher (blind) and allocated into either a virtual reality group (VRG, n = 5) or active control group (ACG, n = 5). Individuals were required to meet the following inclusion criteria: a) dwelling in the LTCH, b) have present preserved capacity of communication (i.e., able to understand and follow commands), and c) endorse subjective cognitive complaints. Exclusion criteria were: a) a positive family history of acute cardiopathy, b) acute musculoskeletal injury hindering exercise performance, and/or c) severe cerebrovascular accident sequelae or neurodegenerative diseases (e. g. dementia). This study was approved by the Ethics Committee of Research of the Montes Claros State University (number 2.398.863).

Participants underwent three exercise sessions on different days to familiarize themselves with the activity, on the fourth day of intervention, evaluations were performed. All assessments were conducted before and immediately after a single session of exercise in the afternoon period. An immediate assessment was chosen to identify an acute neurophysiological and cognitive responses of participants.

2.1. *Frontal cortical activity assessment*

To assess frontal cortical activity, we used mobile Neurosky Mindset (NeuroSky, San Jose, California, USA), with a left frontal electrode (Fp1 area – international system 10/20) stainless steel, with 10 mm diameter, and an earth electrode located on the left ear lobe. Electrical power is obtained and 8000 times amplified. Data show (128 Hz), signal filter and conversion are modulated by a microchip inside the equipment (ThinkGear), which analyses data through the Fourier Transform. The Neurosky Mindset is a valid equipment that presents an acceptable reliability (R = 0.76–0.85) (Rogers et al., 2016). The device was connected via bluetooth to a cell phone Samsung, model J1-SMJ120H/2016 (Samsung, Seoul, South Korea). The electroencephalographic signal was transmitted to the application eegID (Isomer Programming LLC, Hampton, Virginia, EUA). Two assessments were conducted: the first with a 5 min duration, with the participant in a supine position on a stretcher with arms tucked at his/her side, eyes closed and blindfolded, with the encephalographic signal captured with 1 ms reception interval. In the second assessment the participant stood in the same position, with eyes closed and during the same time, however cognitive tests were conducted (short memory term and working memory, semantic fluency and executive function). Both evaluations were conducted immediately before and after the exercise session. Relative power of EEG (RP_{EEG}) referring to delta, theta, alpha and beta brainwaves were analysed.

2.2. *Cognitive Functions (CF)*

Mini-Mental Status Examination (MMSE) (Bertolucci et al., 1994) was used to measure global cognition. To assess semantic fluency/executive function, short-term and working memory we conducted Verbal Fluency (VF) (Brucki et al., 1997) and Weschler Adult Intelligence Scale (WAIS-III) Digit Span (Forward and Backward) (DSF and DSB) (Schroeder et al., 2012) tests.

2.3. *Virtual reality group*

Nintendo Wii game (2D virtual reality) was used during this group's exercise session. We used the following games: Rowing Squat, Penguin Slide and Basic Run Plus of Wii Fit Plus package, with the Wii Balance Board device in the two first exercises and the Heavy Bag, Bump and Set and Dance Basic 1 games of EA Sports Active package: Personal Trainer. These activities require an interaction between the user and the virtual environment through body movements and cognitive abilities simultaneously. Each exercise session lasted 30–45 min in duration, with a 30–60 s interval between games. Participants were only required to complete body weight movements without additional load. A Data Show projector was used to view the game.

2.4. *Active Control Group*

ACG performed the same movement as VRG for 30–45 min with 30–60 s intervals, but without the virtual environment interaction (i.e. no games). All the exercises were counted or timed by the one of the researchers responsible for participants' follow up assessments.

2.5. *Exercise Intensity as moderator*

To verify exercise intensity in each group, participants' heart rate (HR) was assessed by an oximeter Premium Dellamed (Contec, Beijing, China), placed on the index finger of each individual's left hand. Additionally, a biochemical marker of muscle effort (lactate) was analysed before and immediately after the groups' exercise session. To collect lactate, capillary blood samples were obtained from each participant's index finger using an Accu-Chek lancet (Roche, Rio de Janeiro, Brazil). We used a blood drop of the collected blood and we placed it on the field of the test strip BM lactate, and it was posteriorly inserted into the handheld device Accutrend Plus Roche (Roche, Rio de Janeiro, Brazil).

2.6. *Statistical analysis*

Data normality and homoscedasticity were verified using the Shapiro-Wilk and Levene tests, respectively. Data are presented as mean and standard deviation, and minimum and maximum. We performed the estimation of the difference between post- and pre-intervention (Δ) measures of RP_{EEG} and cognitive functions. Demographic variables and characteristics between groups were compared to verify sample homogeneity. To compare Δ (post- minus pre-intervention scores) between groups we used the T Independent Test. Chi-square was used to

Table 1
Control of exercise variables. Mean ± standard deviation.

	VRG			ACG			
	Pre	**Post**	**Δ**	**Pre**	**Post**	**Δ**	*p* BG
Lactate $_{\text{(mmol/l)}}$	3.8 ± 2.2	4.1 ± 2.4	0.3 ± 0.3	3.9 ± 1.6	4.8 ± 2.9	0.88 ± 3.1	0.71
HR $_{\text{(bpm)}}$	78.4 ± 14.6	97.4 ± 5	15.8 ± 17.2	78.8 ± 8.9	93 ± 11.7	14.2 ± 14.9	0.46
SBP $_{\text{(mmHg)}}$	104 ± 15	110 ± 15.8	5.0 ± 8.4	110 ± 12.2	122 ± 17.8	12.0 ± 14.8	0.46
DBP $_{\text{(mmgHg)}}$	60 ± 7.1	64 ± 8.9	3.3 ± 5.2	72 ± 8.3	80 ± 7	8.0 ± 8.4	0.40
OS_2 $_{\text{(\%)}}$	95.8 ± 0.8	96.2 ± 0.8	0.3 ± 0.5	95.2 ± 1.3	95.2 ± 0.8	0.0 ± 1.7	0.64

VRG: virtual reality group; ACG: active control group; HR: heart rate; SBP and DBP: systolic blood pressure and diastolic blood pressure; OS_2: oxygen saturation; *p*BG: Δ comparison between groups.

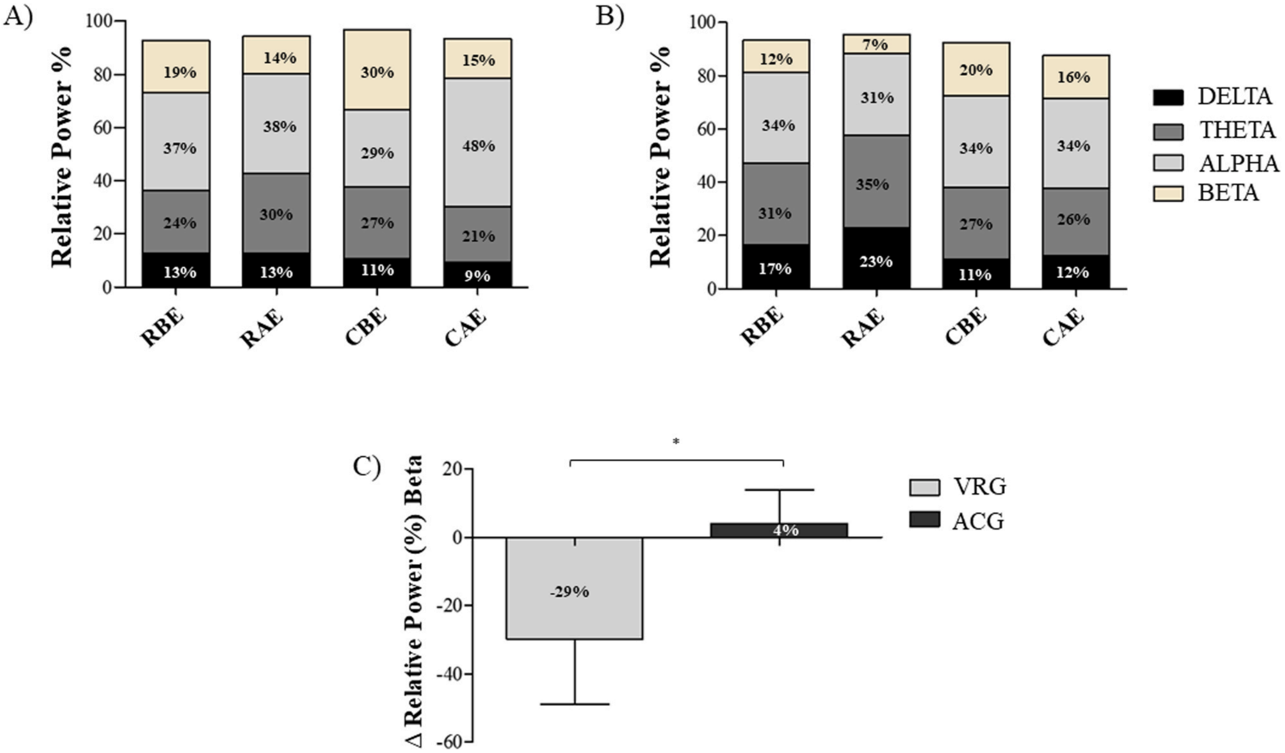

Fig. 1. Left Frontal Cortical Power. A) VRG Relative Power; B) ACG Relative Power; C) Δ Relative Power. RBE: rest before exercise; RAE: rest after exercise; CBE: cognitive assessment before exercise; CAE: cognitive assessment after exercise. *p = 0.007.

frequency analysis. Multiple comparisons were not performed due to the n, which would increase the type I error (Hopkins, 2016). All analyses considered $\alpha \leq 0.05$ as significant. Additionally, we used the calculation of Cohen's Effect Size (ES) (Cohen, 1988). Results of this estimation were classified accordingly to Hopkins (Hopkins, 2002): trivial = 0 and < 0.2; small = 0.2 and < 0.6; moderate = 0.6 and < 1.2; large = 1.2 and < 2; very large = 2 and < 4; almost perfect = 4; and perfect > 4.

3. Results and discussion

There was no difference ($p > 0.05$) in the age, weight, height, years of education, global cognition, and number of drugs. Both groups kept exercise intensity balanced ($p > 0.05$), thus ensuring homogeneity in exercise program prescription (lactate, heart rate, blood pressure) (Table 1).

Fig. 1 (A and B) shows each group RP_{EEG}. When analyzing participants' left prefrontal cortical relative power (difference between post- and pre-intervention = Δ), we verified that VRG had a significant reduction on beta brainwave (−29 ± 18%) compared to ACG (4 ± 9%) ($t = 3.5$; $df = 8$; $p = 0.007$) (Fig. 1C). No other waves were significantly different. In contrast, an effect size (ES) analysis was conducted and showed a small increase on VF performances in VRG (ES = 0.21) and a trivial effect in ACG (ES = 0.13), despite the trivial effect between groups (ES = 0.11). All the other variables presented trivial effect (ES < 0.02).

The main finding was a reduction of RP_{EEG} of beta brainwave in the left prefrontal cortex during the cognitive tests in the VRG compared to ACG. A small effect of improved performance on VF was identified in VRG, thus showing a possible clinical improvement on performances on tasks of semantic fluency/executive function. The comparison between groups also revealed a trivial effect (ES 0.11) of VRG in improving VF. These findings suggest a possible relationship between the reduction of relative power of beta brainwave in the left prefrontal cortex and a small effect of improvement on cognition. However, an ES 0.21 presents a large confidence interval (CI 95% −1.03 to 1.45) limiting any cause-effect relationship.

Older individuals demonstrate increased absolute and relative power of beta brainwave at rest, when compared to younger groups (Holschneider and Leuchter, 1995; Koyama et al., 1997). Regardless of age group, however, healthy individuals should display an increase in beta frontal cortical power during a cognitive test (Oh and Song, 2016). Our findings demonstrate an acute opposite effect of the exergame (i.e, reduced beta brainwave). These findings are in agreement with Tarrant et al. (2018), who showed a reduction in beta brainwave in the anterior

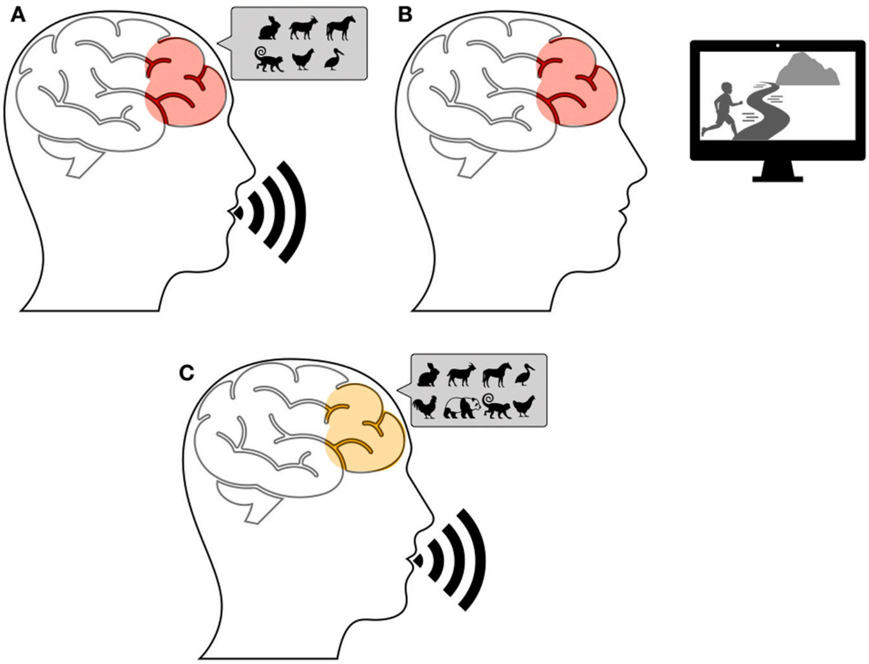

Fig. 2. Exergames stimulation, prefrontal cortex modifications and cognitive performance. A: Person's performance on verbal fluency test (animal category). Red color in the prefrontal cortex indicates high relative power Beta brainwave. B: Person playing exergames. Red color in the prefrontal cortex indicates high relative power Beta brainwave. C: Person's performance on verbal fluency test after exergames session. Yellow color indicates a less relative power Beta brainwave, but the number of animals is higher than previously displayed, showing an ultrafast prefrontal cortex adaptation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

cingulate cortex of individuals undergoing a virtual reality-based intervention. These authors used the LORETA algorithm for EEG to estimate the activation of deeper brain areas. Considering this, it is reasonable to suppose that beta brainwave reduced power might have occurred in different areas of the prefrontal cortex, as the cingulate cortex has connections with the orbitofrontal cortex (Marusak et al., 2016). During the resting state, the beta wave remains low, as there is no participants' cognitive engagement. The same pattern of the beta wave is observed, even after performing an exercise. Therefore, the findings of the present study suggest a possible association between the reduction on RP_{EEG} of beta brainwave in the left prefrontal cortex with cognitive modulation, as a small effect on VF was reached in line with decreased RP_{EEG} of beta brainwave.

A previous study conducted by our group has shown that an intervention of virtual reality-based exercise with exergames had resulted in improved semantic fluency and executive function of institutionalized older adults (Monteiro-Junior et al., 2017a). This investigation corroborates with one of our findings of the present work, which shows that VRG had a small effect on VF performance after the completion of exergames in comparison to ACG. VF abilities are thought to localize to the frontal and temporal lobes (Baldo et al., 2006). Consequently, we suggest that virtual reality-based exercise could enhance cognitive performance due to the modulation of prefrontal cortex during exergames. The cognitive demand during the virtual reality activities would pre-activate the prefrontal cortex, thus generating an ultrafast adaptation (Yuan et al., 2018), which could result into cortical efficiency, causing the decreasing of relative power of beta brainwave during later cognitive request (further cognitive tests post-intervention) (Fig. 2). Furthermore, beta brainwave reduction could be related to a more focused state and less impulsiveness, which would facilitate the resolution of cognitive tasks, and could explain our current results (Makada et al., 2016). The hypothesis could be explained since the increasing in intracellular Ca+ influx, mediated by glutamate and NMDA receptors, activates the cell machinery to express molecular substrates (e.g. transcription factors and proteins) to form LTP. It could be explained in a neurophysiological basis when beta brainwave (12.5–25 Hz) is required during exergames, increasing its relative power. According to the dose of the exergames stimulation (minutes and complexity), a higher beta brainwave relative power would result in LTP in different circuitry of prefrontal cortex. Hence, in the end of the exergames stimulation, the LTP formed would diminish beta brainwave power requirement if a simple cognitive task is required to be solved (e.g. traditional cognitive test to assess attention). In other words, an ultrafast neurophysiological adaptation could occur in the prefrontal cortex, even with a small improvement in cognitive capability to solve simple tasks.

4. Conclusion

Relative power of beta brainwave in the left prefrontal cortex during cognitive task in institutionalized older adults decreased after a single bout of exergames. This finding could be related to an ultrafast prefrontal cortex adaptation mediated through LTP in the brain, but our data are limited and not conclusive. It opens the path for bigger investigations to research deeply the neurophysiological mechanisms that may justify cognitive and functional changes in older individuals undergoing this kind of intervention.

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Declaration of Competing Interest

The authors declare no conflict of interest.

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