




Inhibitory control after aerobic exercise with and without blood flow restriction in older adults

Controle inibitório após exercícios aeróbicos com e sem restrição do fluxo sanguíneo em idosos


Control inhibitorio después del ejercicio aeróbico con y sin restricción del flujo sanguíneo en adultos mayores


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ABSTRACT

Introduction: Regular aerobic exercise (AE) can reduce the cognitive losses typically experienced with aging can be blunted by regular aerobic exercise (AE). AE also induces acute improvement of cognitive function among older adults; and AE practice with blood flow restriction (BFR) adds other benefits to elderly health, such as improvements in aerobic fitness, and increase in muscle mass and strength, however, it is not clear which EA protocol is more efficient to cognitive function. **Objectives:** Thus, the aim of this study was to compare AE protocols with and without BFR on the inhibitory control of the elderly. **Methodology:** Twenty-one elderly performed the Stroop test before and after three AE sessions in a repeated measure, cross-over design: AE with high load (70% VO₂max), AE with low load (40% VO₂max), and AE with blood flow restriction (AE-BFR) BFR (40% VO₂max and 50% of BFR). **Results and discussion:** There was no significant effect from experimental sessions on cognitive function, assessed by inhibitory control in Stroop test. Perhaps, the load applied was not proper to stimulate cognitive function improvements, as seen the moderate loads have been more efficient to increase cerebral blood flow, among other physiological mechanisms encompassed. **Final Considerations:** Moreover, we observed very heterogeneous responses among individuals and sessions, suggesting that future research also considers biological individuality.

Keywords: Cognition. Exercise. Elderly Health. Stroop Test. Inhibitory control.

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RESUMO

Introdução: As perdas cognitivas tipicamente experimentadas com o envelhecimento podem ser atenuadas por exercícios aeróbicos (EA) regulares. EA também induz melhora aguda da função cognitiva em idosos; e a prática de EA com restrição de fluxo sanguíneo (RFS) agrega outros benefícios à saúde do idoso, como melhorias na aptidão aeróbia e aumento da massa e força muscular. No entanto, não está claro qual protocolo de EA é mais eficaz para a função cognitiva. **Objetivos:** Assim, o objetivo deste estudo foi comparar diferentes protocolos de EA com e sem RFS no controle inibitório de idosos. **Metodologia:** Vinte e um idosos realizaram o teste de Stroop antes e após três sessões de EA em medida repetida, desenho cruzado: EA com alta carga (70% VO₂máx), EA com baixa carga (40% VO₂máx) e EA com RFS (40% VO₂máx e 50% do RFS). **Resultados e discussão:** Não houve efeito significativo das sessões experimentais na função cognitiva avaliada pelo controle inibitório no *Stroop Test*. Talvez, as cargas aplicadas não tenham sido adequadas para estimular melhorias no controle inibitório, visto que as cargas moderadas têm sido mais eficientes para aumentar o fluxo sanguíneo cerebral, entre outros mecanismos fisiológicos. **Considerações Finais:** Além disso, observamos respostas bastante heterogêneas entre indivíduos e sessões, sugerindo que pesquisas futuras considere também a individualidade biológica.

Palavras-chave: Cognição. Exercício. Saúde do Idoso. Teste de Stroop. Controle inibitório.

RESUMEN

Introducción: El ejercicio aeróbico regular (EA) puede reducir la pérdida cognitiva tipicamente experimentada durante el envejecimiento. EA puede también inducir mejora en la función cognitiva entre adultos mayores, además, la práctica de restricción de flujo sanguíneo (RFS) agrega otros beneficios para la salud en los ancianos, así como mejoras en la aptitud aeróbica, aumento de la masa muscular y la fuerza, sin embargo, no está claro qué protocolo de EA es más eficiente para la función cognitiva. **Objetivos:** El objetivo de este estudio fue comparar los protocolos de EA con y sin RFS en el control inhibitorio de los ancianos. **Metodología:** Veintiún ancianos realizaron la prueba de Stroop antes y después de tres sesiones de EA en medida repetida, diseño cruzado: EA con carga alta (70% VO₂max), EA con carga baja (40% VO₂max) y EA con restricción del flujo sanguíneo (EA-RFS) RFS (40% VO₂max y 50% de RFS). **Resultados y discusión:** No hubo efecto significativo de las sesiones experimentales sobre la función cognitiva, evaluada por el control inhibitorio en la prueba de Stroop. Quizás, la carga aplicada no fue la adecuada para estimular mejoras en la función cognitiva, ya que las cargas moderadas han sido más eficientes para aumentar el flujo sanguíneo cerebral, entre otros mecanismos fisiológicos englobados. **Consideraciones finales:** Además, nosotros observamos respuestas muy heterogêneas entre individuos y sesiones, lo que sugiere que para futuras investigaciones también se debe considerar la variabilidad biológica.

Palabras Clave: Cognición. Ejercicio. Salud del Anciano. Prueba de Stroop. Control inhibitorio.

INTRODUCTION

While the white and grey matter losses in frontal, parietal, and temporal areas are evident with aging, they are attenuated in patients with higher cardiovascular fitness levels (COLCOMBE *et al.*, 2003). The chronic benefits from aerobic exercise (AE) training on the cognitive function, including executive function, cognitive control, visuospatial memory, and reaction time, are entirely elucidated (COLCOMBE *et al.*, 2003). However, the acute effects of exercise are still inconclusive as seen many protocols have acutely increased elderly cognitive functions, and some protocols have shown null effects (ALVES *et al.*, 2012; BARELLA *et al.*, 2010; PONTIFEX *et al.*, 2009; VASQUES *et al.*, 2011). Studies using Stroop test have showed improvement in inhibitory control, a component of executive function in younger adults after walking (SUGIMOTO *et al.*, 2021). Possible mechanics considered are increase cerebral neural activation, greater metabolic response and muscle hypoxia mediate by sympathetic nervous system via chemoreceptors and metaboreceptors (MANINI; CLARK, 2009).

Recently, low-load resistance exercise has increased attention, reaction time, and inhibitory control in healthy elderly (SARDELI *et al.*, 2018a). In the same study, resistance exercise with blood flow restriction (BFR) has not led to such benefits as low-load resistance exercise. However it is noteworthy that the responses among individuals to BFR was very heterogeneous. Since there is an ideal increase in sympathetic modulation to improve cognitive function; it is possible that the BFR exercise led to exacerbated increases in sympathetic modulation, not just by the accumulation of metabolites in the muscle but also by possible higher anxiety level (not analysed) considering it was a new type of exercise for the participants and different of usual exercise types (MURRAY; RUSSONIELLO, 2012; SARDELI *et al.*, 2018a).

In general, aerobic exercise (AE) requires the contraction of large portion of muscles at moderate intensity, which implicates in a more dynamic blood circulation (moderate HR increases, efficient venous return, increase in stroke volume, without exacerbating elevations in blood pressure) compared to a more static pattern of resistance exercise (ROWELL, 1992). This different circulatory patterns has also been observed comparing AE and resistance exercise with BFR, and thus this last one might hold vast potential to stimulate cognitive function (SARDELI *et al.*, 2021).

Alves *et al.* (2012) showed similar increases after resistance exercise and AE, while Pontiflex *et al.* (PONTIFEX *et al.*, 2009) showed AE could be more efficient than resistance exercise for improving reaction time and in a task requiring executive function. They suggested these differences were due to the different metabolic and cardiovascular demands between the exercise modalities. Furthermore, in the study testing resistance exercise with and without BFR in the

elderly (SARDELI *et al.*, 2018a), there were correlations between cardiac output and cardiac autonomic modulation indexes with changes in cognitive function. It suggested that the improvement found after low-load and high-volume resistance exercise was due to higher cardiac output and lower parasympathetic modulation following this more dynamic type of resistance exercise (SARDELI *et al.*, 2018a). Therefore, since AE is essentially dynamic, we expect even better results with AE-BFR.

Besides the high dynamic component of AE, which could explain its advantage over resistance exercise considering cognitive function, the AE with BFR can improve aerobic fitness and muscle mass following a period of training (ABE *et al.*, 2006, 2010). These beneficial chronic effects increase the ecological validity of research about this type of exercise. Whether the acute AE with blood flow restriction (AE-BFR) could increase inhibitory control is still unknown and, thus, we aim to compare the acute effects of AE with and without BFR on inhibitory control in healthy elderly.

Additionally, recent literature has shown that lactate is the main energy substrate of the brain during exercise; thus, the increase in lactate levels in the brain and blood, resulting from physical exercise, seems to improve executive function (Cho *et al.*, 2020). In this perspective, considering that high-intensity aerobic exercises (75% of peak aerobic capacity) seem to increase (in greater magnitude) the lactate concentration when compared to low-intensity aerobic exercises, with and without blood flow restriction, in physically active subjects (age 18 to 35 years) (Kim *et al.*, 2016), it is necessary to investigate the acute effects of aerobic exercise, with and without blood flow restriction, on cognitive function in the elderly.

METHOD

SUBJECTS

Twenty-one healthy sedentary elderly enrolled for this survey. Before inclusion, a clinical examination was carried out. Subjects were excluded if they had less than 60 years old, any neurological condition, coronary artery disease, hypertension, diabetes mellitus (insulin-dependent), chronic obstructive pulmonary disease, limiting osteoarticular diseases, any type of neurological disorder current smoker, BMI > 30kg/m² or if they use any medication that could interfere with the physiological responses of evaluations. The participants signed the informed consent of this research, approved by the ethics committee of the University of Campinas (1.198.571). A previous study of our group (SARDELI *et al.*, 2018b) with almost the same participants found significant differences ($p < 0.05$) between the effects of different resistance exercise protocols on Stroop

test. Thus, we assumed, the same number of participants would ensure 95% power for this study.

STUDY DESIGN

The three AE sessions were performed in a cross-over design with one-week intervals among them, always in the same morning time considering the circadian cycle influences. All experimental sessions were conducted in a temperature and humidity-controlled environment in a quiet place to avoid external interference on in data collection. Participants were instructed to avoid alcohol, stimulant drinks (coffee or tea), sleep well a day before procedures and refrain from exercise for at least 72h. At the beginning of experimental sessions, the primary health conditions of the participants were verified, and the sessions were postponed whenever necessary.

EXPERIMENTAL PROTOCOL

AE protocols were performed on a treadmill for 20 minutes with continuous load, defined as: 70% of VO_2 max (high load- HL), 40% of VO_2 max (low load- LL), and 40% of VO_2 max with 50% BFR (LL-BFR). The BFR pressure was set as 50 % of systolic blood pressure at rest was held during the entire LL-BFR protocol (Ferreira *et al.*, 2017). Stroop test were applied immediately before protocols and 30 min after the end of AE session.

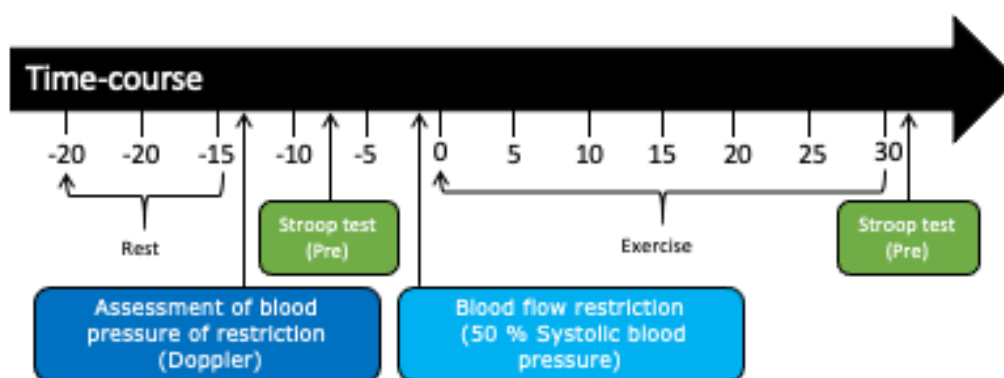


Figure 1 – Experimental protocol.

ASSESSMENTS

CARDIORESPIRATORY EVALUATION

The maximum test was performed on a treadmill (Quinton TM55. Bothell, Washington, EUA) equipped with a gas analyzer (CPX, Medical Graphics, St. Paul, Minnesota, USA) where the gas exchange was analyzed continuously, breath by breath, to determine the VO_2 maximum. The protocol started with a 4 km/h (warming up) for 2 minutes, the speed was increased 0.3 km/h every 30

seconds until the volitional exhaustion and cooldown started at 5km/h with decrements of 1 km/h each minute until the 4th min recovery (Libardi *et al.*, 2011). VO_2 max. was determined for the following criterion: $\text{RER} > 1.1$ $\text{PSE} > 17$, $\text{bpm} \pm 10$ heart rate predicted by age ($220 - \text{age}$). The mean oxygen consumption at the 30 seconds before volitional exhaustion was used to determine the VO_2 max.

DETERMINATION OF INDIVIDUAL BFR

Following 5 minutes of rest in the supine position, a vascular Doppler probe (DV-600; Marted, Ribeirão Preto, São Paulo, Brazil) was placed over the tibial artery to capture its auscultatory pulse while a standard blood pressure cuff was positioned in the quadriceps inguinal fold region. Cuff was inflated up to the point at which the auscultatory pulse was interrupted, and the systolic blood pressure was defined as 2 mmHg above the point of restoration of this pulse (Ferreira *et al.*, 2017; Laurentino *et al.*, 2008). We measured the individual BFR pressure prior to all sessions, regardless of their exercise session.

STROOP TEST

Cognitive functions, including a component of executive function (inhibitory control) and reaction time were evaluated by the computerized version of Stroop test TESTINPACS® (STROOP, 1935), and the protocols are detailed elsewhere (Sardeli *et al.*, 2018a). Participants were instructed to use the forefingers of both hands to press one of the two options of the keyboard key ([←] or [→]), and previous to the experimental AE protocols they performed a familiarization test. Stroop test was composed of three steps. In step 1 the participants had to choose the right name for the color displayed on the screen and it was used to warm up the participants as well as to evaluate their color perception. In step 2 participants had to choose the right name for the color writing with the letters colored always in white (neutral stimuli). In step 3 (incongruent stimulus) participants had to choose the right name of the color of the word letters instead of the name of the color written. The test was performed pre and post-exercise. The software registered the number of errors and reaction time to each stimulus (measured in milliseconds). There were 12 random stimuli in each step. Mean reaction time and overall number of errors were registered for each step (I,II and III) as shown in Figure 2.

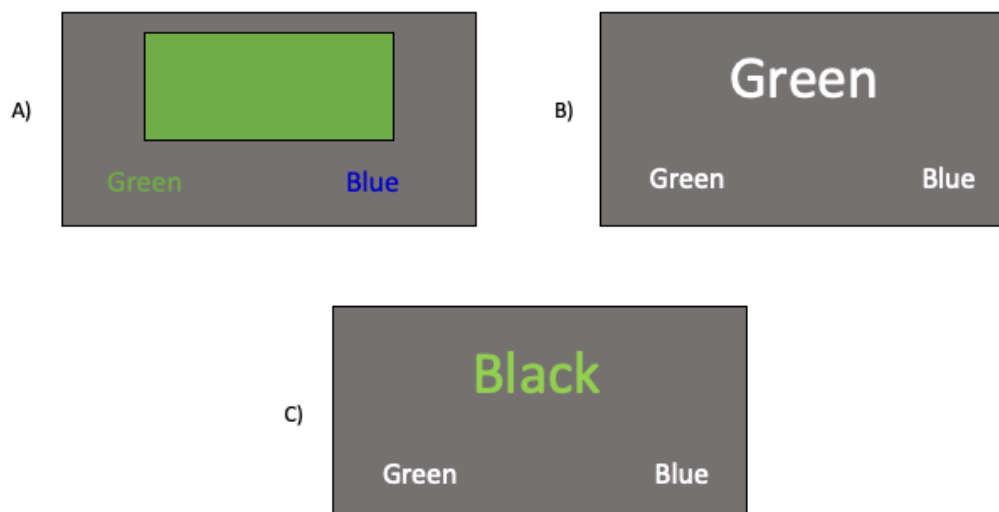


Figure 2 – Stroop test examples - A) color condition; B) word condition; C) Incongruent condition (required inhibitory control do deal with).

STATISTICAL ANALYSIS

Shapiro Wilk test showed the data were not normally distributed. Analysis of Mixed model was used, time (pre and post) and protocols (LL, LL-BFR and HL) set as fixe effects while each subject as a random factor. Effect size between moments was calculated. Delta of responses were calculated based on the mean of each group (LL, LLBFR and HL) post – pre of Stroop data (Reaction time and number of errors). All analyses were performed using R programming language (Vienna, Austria, 2015) Level of significance was set as $p \leq 0.05$. Data are presented in mean \pm standard deviation.

RESULTS AND DISCUSSION

Sample characteristics are described in table 1. There was no effect of time, condition, or interaction between Time x Condition for the number of errors and Reaction Time (table 2). Effect size was larger for LL (-0.83) in reaction time Stroop task III, while for HL was medium (-0.26) and small (0.18) for LL-BFR. Considering the effects of exercise were widely heterogeneous, we described individuals' delta of responses in step 3 (incongruent stimulus) for each AE protocol (Figure 3).

Table 1 - Sample characteristics

N	24 (9♂/12♀)
Age (years)	63.7 ± 4.19
Educational level	
Basic (8 years)	5
High school (11 years)	4
Graduation (15 years)	12
Anthropometry	
Body mass (Kg)	64.29 ± 11.69
Height (m)	1.60 ± 0.08
BMI (kg/m ²)	24.68 ± 2.78
Aerobic capacity	
VO ₂ max	24.88 ± 5.92

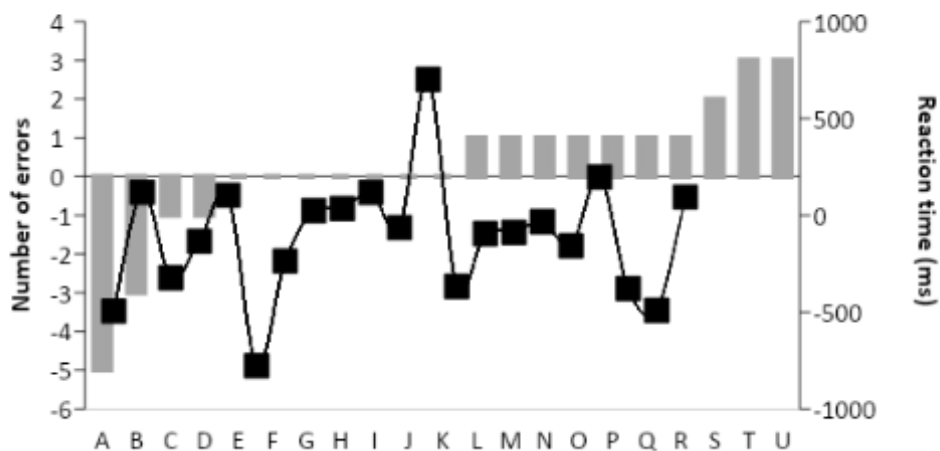
Data are shown in mean ± standard deviation. BMI: Body mass index VO₂max: Maximum oxygen consumption.

Table 2. The number of errors and reaction time pre and post-experimental sessions.

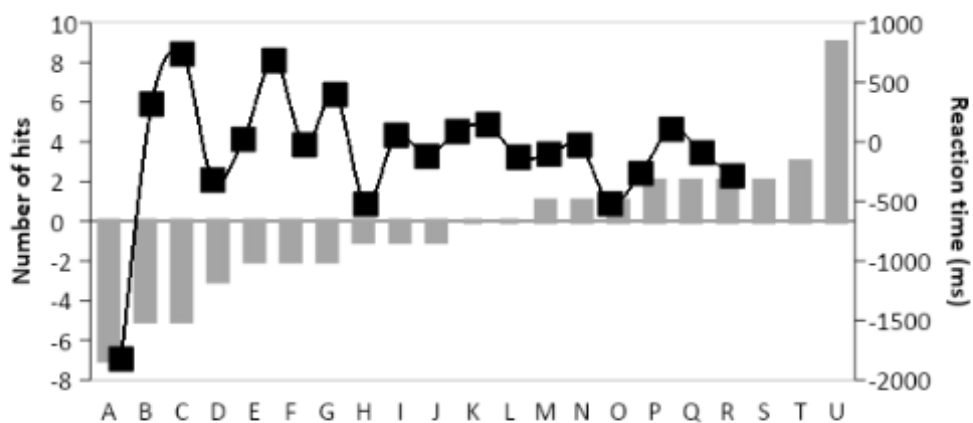
	HL Pre	Post	EF	LL Pre	Post	EF	LL-BFR Pre	Post	EF
Number of errors									
Step I	0.1 (0.5)	0.1 (0.3)	-0.11	0.2 (0.4)	0.2 (0.5)	-0.11	0.3 (0.7)	0.2 (0.4)	-0.16
Step II	0.4 (0.8)	0.4 (0.6)	-0.11	0.6 (1.4)	0.5 (0.8)	-0.21	0.4 (0.7)	0.4 (0.6)	0.0
Step III	3.8 (4.7)	4.0 (4.4)	0.05	4.1 (4.4)	3.8 (4.2)	-0.06	3.9 (4.0)	3.2 (4.1)	-0.16
Reaction time									
Step I	1766.3 (431.5)	1636.4 (271.2)	-0.36	1740.7 (371.7)	1662.3 (263.1)	-0.24	1735.1 (364.8)	1690.5 (300.0)	-0.13
Step II	1874.0 (455.3)	1840.2 (346.0)	-0.36	1937. (364.0)	1791.4 (265.2)	-0.46	1905.8 (349.2)	1795.2 (365.3)	-0.30
Step III	2338.4 (852.4)	2175.4 (751.7)	-0.83	2338.4 (795.9)	2144.8 (579.7)	-0.26	2311.6 (665.5)	2337.1 (622.1)	0.18

Data are shown in mean ± standard deviation. HL: High load; LL: Low load; LL-BFR: Low load with blood flow restriction; EF: Effect Size (Cohen's d); *P-values <0.05 would be reported here.

A



B



C

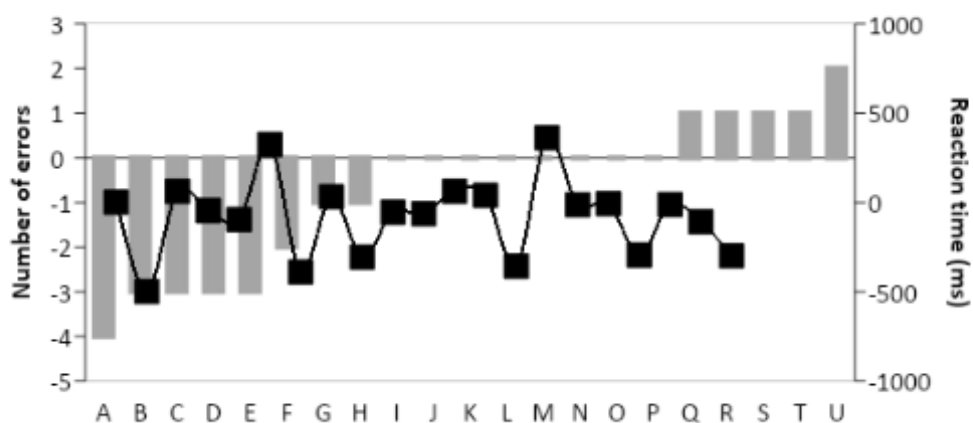


Figure 3. A: Delta of change of the number of errors and reaction time step 3 for each participant on HL group. B: Delta of change of the number of errors and reaction time step 3 for the participant on LL group. C: Delta of change of the number of errors and reaction time step 3 for participant on LL-BFR group. Grey bars represent number of errors. Black lines represent the reaction time.

The present study aimed to address which AE protocol, with or without BFR was the most effective to improve cognitive function. The three protocols tested herein showed no effects on the elderly. There was no significant change in neither number of errors nor reaction time on Stroop test, even though effect size for LL and HL was negative for time Stroop III. If these effects were confirmed, they would suggest a better inhibitory control. However, there was a high variability of responses among participants and future studies need to confirm this effect. Additionally, AE-BFR was unusual for participants and it might have caused different psychological effects and cardiovascular stress among different individuals (SARDELI *et al.*, 2017).

It is not clear why we did not observe improvements with the aerobic exercise protocols, considering executive functions (usually inhibitory control and reaction time assessed by Stroop test) seem to be easily improved after exercise in other studies (HOGERVORST *et al.*, 1996; YANAGISAWA *et al.*, 2010).

Kashihara *et al.* (2009) suggested AE benefits cognition because of the increase of cerebral blood flow (CBF) and greater glucose, oxygen, and energetic substrates delivery, neurotransmitter release, humor mediators as β -endorphin and serotonin, adrenaline release, and neurotrophic factors as Brain-Derived Neurotrophic Factor (BDNF) and finally autonomic nervous system modulations. They complement that all these changes necessary for cognitive function improvement after exercise only manifest when AE is performed at moderate intensity, around the anaerobic threshold. Cardiac autonomic modulation and CBF, stimulate improvement in cognitive functions through an ideal intensity, where either very low stimulus or very high showed no effects or even impaired the cognitive function (MURRAY; RUSSONIELLO, 2012; SECHER *et al.*, 2008). In fact, some studies had shown improvements in cognition when AE was performed at moderate intensities, such as at 40 – 60 % of maximum heart rate by older adults with mild cognitive impairment (DAVIS *et al.*, 2013) and at 11-13 rating of perceived exertion in healthy elderly (HÅKANSSON *et al.*, 2017). Moreover, Bender *et al.* (BENDER; Mcglynn, 1976) showed increments in reaction time worst score) according to load increments at 41.7%, 57.7%, 75 %, and 93 % of the reserve heart rate, after exercise reaction time was significantly lower than the pre-test showing an inverse relationship between load and improvement on cognitive function. As seen, the present study has tested very low or high intensity (40% or 70% of VO_2max); perhaps none of the protocols were performed at the ideal load for cognition stimulation.

BDNF has been associated with improved cognitive function after a single bout of exercise through the improvement of neural activity. (DINOFF *et al.*, 2016) In humans, exercise mediate the BDNF release, and the intensity of exercise is associated with the magnitude of BDNF increase (FERRIS *et al.*, 2007). BDNF has been found in the anterior cingulate cortex, an area responsible for conflict resolution, information selection, and processing for the

established goals demanded by tasks (PARDO *et al.*, 1990). BDNF modulates excitatory neurotransmitter release from the presynaptic to the post synaptic, facilitating neural depolarization. Although, BDNF availability and neurotransmitter release are intensity dependent, we would expect to see at least an improvement in cognition following HL through BDNF modulation, therefore, another factors not measures would also mediate this phenomenon.

The present study was the absence of assessment of humor, affection, and other psychological changes that could mediate exercise effects on cognitive function (KASHIHARA *et al.*, 2009; MOGLE *et al.*, 2017). Nevertheless, the RPE results did not show different effects between these LL and LL-BFR protocols as a previous study of our group showed (FERREIRA *et al.*, 2017), implying that AE with and without BFR did not influence the different levels of fatigue that in turn impacted in cognitive function results. Thus, it was a limitation of the present study that we did not evaluate the state of mental fatigue before and after exercise training session, blood glucose or lactate measures as an indicator of exercise intensity.

FINAL CONSIDERATIONS

This study compared different acute aerobic exercise protocols, high load, low load, and low load with BFR in older adults. Any protocol reduced reaction time or the number of errors. Maybe intensity and volume of exercise used in this study were insufficient to promote effects on cognitive function. Also, the absence of cognitive impairment among the sample studied should be taken into consideration. In this way, future studies should investigate the physiological mechanisms associated with this phenomenon, chasing to understand the persistent contradictory findings.

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NOTES

CONFLICT OF INTEREST

Authors have no conflicts of interest, including specific financial interests and relationships and affiliations relevant to the topic or materials discussed in the manuscript.

AUTHORSHIP

Authors declare that they participated in a significant way in the construction and formation of this study, having, as authors, public responsibility for its content, as they directly contributed to the intellectual content of this work and obeyed the authorship requirements.

Wellington Martins dos Santos - Analysis/interpretation (responsible for the statistical analysis, evaluation, and presentation of the results); Literature survey (participated in the bibliographical research and the article survey); Redaction (responsible for writing a substantial part of the manuscript); Critic review (responsible for the review of the intellectual content of the manuscript before the final presentation).

Amanda Veiga Sardeli - Conception and development (since the idea to the investigation or article, created the hypotheses); Methodological design (planning of the methods to generate the results); Supervision (responsible for the organization and execution of the project and the writing of the manuscript); Collection and treatment of the data (responsible for the experiments, patients, data organization); Analysis/interpretation (responsible for the statistical analysis, evaluation, and presentation of the results); Literature survey (participated in the bibliographical research and the article survey); Redaction (responsible for writing a substantial part of the manuscript); Critic review (responsible for the review of the intellectual content of the manuscript before the final presentation).

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Mara Patrícia Traina Chacon-Mikahil - Conception and development (since the idea to the investigation or article, created the hypotheses); Methodological design (planning of the methods to generate the results); Critic review (responsible for the review of the intellectual content of the manuscript before the final presentation).

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