Cognitive and physical effects of a multicomponent training in elderly adults: A pilot study

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UMinho | 2020

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Dissertação de Mestrado
Mestrado em Psicologia Aplicada

Trabalho efetuado sob a orientação da
Doutora Anabela Silva Fernandes

setembro de 2020

FUNDING AND AUTHOR CONTRIBUTION

We would like to express our most gratitude to all participants involved in this study. This study was partially conducted at the Psychology Research Centre (PSI/01662), University of Minho, and supported by the Portuguese Foundation for Science and Technology and the Portuguese Ministry of Science, Technology and Higher Education (UID/PSI/01662/2019), through the national funds (PIDDAC); and at Research Center in Physical Activity, Health and Leisure (FCT/ UIDB/00617/2020; POCI-01-0145-FEDER-031808). This study was supported by the Portuguese Ministry of Science, Technology and Higher Education through national funds and co-financed by FEDER through COMPETE2020 under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007653).

This study was funded by Bial Foundation (#286/16), FCT (NORTE-01-0145-FEDER-032152, POCI-01-0145-FEDER-028682, POCI-01-0145-FEDER-031808) and by Instituto Português do Desporto e Juventude. This study was supported by the Portuguese Foundation for Science and Technology and the Portuguese Ministry of Science, Technology and Higher Education, through the national funds, within the scope of the Transitory Disposition of the Decree No. 57/2016, of 29th of August, amended by Law No. 57/2017 of 19 July and previously through the fellowship grant SFRH/BPD/107732/2015.

STATEMENT OF INTEGRITY

I hereby declare having conducted this academic work with integrity. I confirm that I have not used plagiarism or any form of undue use of information or falsification of results along the process leading to its elaboration.

I further declare that I have fully acknowledged the Code of Ethical Conduct of the University of Minho.

Signature: Marisa Ferreira

Efeitos cognitivos e físicos de um treino multicomponente em idosos: Um estudo-piloto

Resumo

A população mundial está a envelhecer. O envelhecimento bem-sucedido propõe que a atividade física e o exercício físico possam ser protetores da cognição e do cérebro. No entanto, a intensidade da atividade física e as características do exercício físico (duração, modalidade ...) ideais para maximizar os efeitos cognitivos não são claros. Este estudo-piloto tem como objetivos (1) clarificar os efeitos cognitivos, emocionais e de aptidão física de uma intervenção com treino multicomponente em idosos da comunidade e compará-los com um grupo de controlo ativo; (2) explorar as associações entre função cognitiva e aptidão física. Foi conduzida uma intervenção quasi-experimental double-blind, no Norte de Portugal com 19 participantes com idade >60 anos, distribuídos por ordem de inscrição. A intervenção multicomponente incluiu exercícios aeróbicos, de força, alongamento e equilíbrio, três vezes por semana durante 50 minutos, por 33 semanas. A intervenção de controlo ocorreu uma vez por semana, com menor intensidade. Os participantes foram avaliados antes e depois da intervenção nos níveis de atividade física (actigrafia), função neurocognitiva, estado emocional, aptidão cardiorrespiratória (VO_{2pico}) e antropometria (DEXA). O treino multicomponente foi eficaz em aumentar a atividade física moderada-a-vigorosa e diminuir o tempo sedentário, em comparação com o grupo controlo. Não foram encontrados efeitos significativos na antropometria ou no estado emocional. O grupo multicomponente diminuiu significativamente o VO_{2pico}, portanto, este treino não foi eficaz a aumentar a aptidão cardiorespiratória. Os dois grupos pioraram a performance na fluência semântica e o grupo multicomponente na memória de trabalho, pelo que o treino multicomponente não foi eficaz em melhorar ou manter as funções neurocognitivas. Numa análise secundária personalizada, variações no VO_{2pico} foram associadas com variações na memória a curto e longo-prazos. Contrariamente, variações na antropometria não se correlacionaram com variações cognitivas. A hipótese de aptidão cardiorespiratória pode contribuir para explicar os resultados. Com as aprendizagens do estudo-piloto, refletimos sobre diretrizes para um futuro ensaio clínico randomizado.

Palavras-chave: aptidão física, cognição, exercício físico, idosos, treino multicomponente

Cognitive and physical effects of a multicomponent training in elderly adults: A pilot study

Abstract

World's population is aging. Successful aging proposes that physical activity and physical exercise may be protective for cognition and the brain. The intensity of physical activity and the characteristics of physical exercise (duration, modality…) that are optimal to maximize cognitive effects are yet to be discovered. Current investigation aims at (1) clarifying cognitive, emotional and physical fitness effects of a multicomponent training intervention in community-dwelling elderly and compare them with an active control group; (2) exploring the association between cognitive function and physical fitness. A double-blind quasi-experimental intervention was conducted with 19 participants aged>60year from the North of Portugal, distributed by order of registration. Multicomponent intervention included aerobic, strength, stretching and balance exercises thrice a week for 50min for 33-weeks. Control intervention occurred once a week with less intensity. Participants were assessed at baseline and after-intervention in physical activity levels (actigraphy), neurocognitive function, emotional status, cardiorespiratory fitness (VO_{2peak}) and anthropometry (DEXA). Multicomponent training was effective in improving moderate-to-vigorous physical activity and diminishing sedentary-time, compared to control group. It presented no significant effects for anthropometry or emotional status. Multicomponent group significantly decreased VO_{2peak}, hence multicomponent training was not effective in improving cardiorespiratory fitness. Both groups significantly decreased performance in semantic fluency and multicomponent group significantly decreased performance in working memory. Thereby, multicomponent training was not effective at improving or maintaining neurocognitive functions. In a secondary-personalized analysis, variations in VO_{2peak} were associated with variations in short-term and long-term memory. Contrarily, variations in body composition were not. Cardiorespiratory fitness hypothesis may contribute to our results. With learning from the pilot study, guidelines for future randomized-controlled trials are suggested.

Keywords: cognition, elderly, physical exercise, physical fitness, multicomponent training

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List of Abbreviations

ACSM: American College of Sports Medicine

BMD: Bone Mineral Density

BMI: Body Mass Index

CG: Control Group

CI: Confidence Interval

CRF: Cardiorespiratory Fitness

DEXA: Dual Energy X-ray Absorptiometry

EF: Executive Functions

FADEUP: Faculdade de Desporto da Universidade do Porto

GXT: Graded Exercise Test

HR: Heart Rate

HR_{max}: Maximal Heart Rate

HRR: Heart Rate Reserve

LPA: Light Physical Activity

MCT: Multicomponent Exercise Training

MCG: Multicomponent Exercise Training Group

MPA: Moderate Physical Activity

MVPA: Moderate to Vigorous Physical Activity

PA: Physical Activity

η^2: Partial Eta Squared

PE: Physical Exercise

RCT: Randomized Control Trial

RER: Respiratory Exchange Ratio

RM-ANCOVA: Repeated Measures Analysis of Covariance

SED: Sedentary Time

VCO_2: Volume of Carbon Dioxide Production

VO_2: Volume of Oxygen Uptake

VO_{2max}: Maximal Oxygen Uptake

VO_{2peak}: Peak Volume of Oxygen

WHO: World Health Organization

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Cognitive and Physical Effects of a Multicomponent Training in Elderly Adults: A Pilot Study

The world's population is aging and the rate at which it is happening is accelerating (United Nations. Department of Economic and Social Affairs Population Division, 2017). In 2018, 21.5% of the Portuguese population was at least 65 years old (Eurostat: Statistics Explained, 2018). Moreover, by 2050, 2.1 billion people will be at least 60 years and Portugal will be the third oldest country worldwide, with 41.7% of its population aged above 60 (United Nations. Department of Economic and Social Affairs Population Division, 2017).

As aging has become a worldwide issue, two different approaches have emerged. First is finding hallmarks of cognitive and brain aging, second is successful aging.

Hallmarks of cognitive aging refer to declines in memory (mainly episodic and prospective memory), executive functions (EF) (working memory, attention, task-switching, processing speed), language and visuospatial function (Alexander et al., 2012; Blazer et al., 2015; Erickson et al., 2015; Grady, 2013). Brain changes accompanying respective cognitive decline include decreases in synapses' integrity - changes in number and function, primarily prefrontal cortex and hippocampus; changes in neurotransmission (Blazer et al., 2015) and brain atrophy, namely reduced volume of gray matter, reduced integrity of white matter and expansion of the cerebrospinal fluid spaces (Erickson et al., 2015; Fjell et al., 2013; Grady, 2013; Johansen-Berg & Rushworth, 2009; Raz et al., 1997). Nonetheless, cognitive and brain changes are idiosyncratic with enormous inter and intra-individuals variability (Blazer et al., 2015; Erickson et al., 2011; Raz et al., 1997). Research in characteristics of clinical cognitive decline and its possible treatments (Gale et al., 2018; Liang et al., 2019; Lipnicki et al., 2017) points to physical activity (PA) as useful therapeutic tool for dementia's associated decline (Chodzko-Azjko et al., 2009; Devenney et al., 2017; Erickson et al., 2011, 2015; Gomes-Osman et al., 2018; Grande et al., 2020). While dementia is still incurable, preventing cognitive decline and promoting successful aging have become a priority (Gomes-Osman et al., 2018; Grande et al., 2020; Jia et al., 2019; Liang et al., 2019; Smith, 2019; Tisher & Salardini, 2019).

Successful aging, firstly proposed by Rowe and Kahn (1987), attributes major age-associated declines to lifestyle behaviors, habits, diet and psychosocial factors extrinsic to the aging process. Clarification of what lifestyle and behavioral factors differentiate a pathway of successful aging from a pathway of clinical cognitive decline are being investigated. Research in successful brain aging has been trying to distinguish individuals with less cognitive loss or fewer markers of brain pathology/dysfunction from their age-matched counterparts, and relate these markers to lifestyle and behavioral factors (Kaup et al., 2011; Thielke & Diehr, 2012). Simultaneously, cognitive brain health is being promoted, representing the capacity to remember, learn, plan, concentrate and maintain a clear active mind (Gomes-Osman et al., 2018). PA has been investigated as a primary motor of it since it aims at improve or, at least, maintain neurocognitive functions, counteract effects of cognitive decline and reduce the risk of cognitive decline or dementia (Bherer et al., 2013; Chodzko-Azjko et al., 2009; Cotman & Berchtold, 2002; Gomes-Osman et al., 2018; Voss et al., 2019; Yaffe et al., 2009).

Given the low cost and initial cognitive benefits, World Health Organization (WHO; 2010, 2015, 2019) recommended PA practice to adults with normal cognition to promote healthy aging and reduce the risk of cognitive decline. For adults over 65, the weekly recommendation is of at least 150 minutes of moderate-intensity aerobic PA; 75 minutes of vigorous-intensity aerobic PA or a combination of both. Unfortunately, only 35% of Portuguese adults >64 years follow PA recommendations (Baptista et al., 2012), raising concerns of cognitive, brain and general health.

PA and PE are distinct concepts sometimes used interchangeably in literature. PA is defined as “any bodily movement produced by skeletal muscles that results in energy expenditure substantially” (Caspersen et al., 1985, p.126). It can be classified into levels: sedentary time (SED); light PA (LPA); moderate PA; vigorous PA or moderate-to-vigorous (MVPA) (Migueles et al., 2017; Troiano et al., 2008). It encompasses leisure time, transportation as walking or cycling, occupational, household chores and sports or planned exercise (American College of Sports Medicine [ACSM], 2018; Caspersen et al., 1985; WHO, 2010). PE is defined as planned, structured, repetitive, aiming at maintaining or improving at least one component of physical fitness (ACSM 2018; Caspersen et al., 1985).

Physical fitness is the “ability to carry out tasks with vigor and alertness, without fatigue and with ample energy to enjoy leisure-time pursuits and to meet unforeseen emergencies, constituting a set of attributes that people have or achieve” (ACSM, 2018, pp. 49-50). Is influenced by regular participation in PE (Chodzko-Azjko et al., 2009) and comprises skill-related fitness and health-related fitness (ACSM 2018; Caspersen et al., 1985). Cardiorespiratory fitness (CRF) (aerobic fitness or aerobic capacity) is one of the most investigated health-related components. Aerobic fitness represents the ability to perform moderate-to-high intensity exercise for prolonged periods of time. It is based on the functional state of the respiratory, cardiovascular and musculoskeletal systems since during PA sustained practice, the two first provide the required oxygen to the musculoskeletal (ACSM 2018; Caspersen et al., 1985). The gold standard measure of CRF is Maximal Oxygen Uptake (VO_{2max}), that represents (usually in relative to body weight) maximal volume of oxygen consumed per unit time ($mL \cdot kg^{-1} \cdot min^{-1}$). VO_{2max} entails the achievement of an individual's true physiologic limit since volume of oxygen fails to increase (representing a plateau) with progressive workloads, in a graded exercise test (GXT) (ACSM, 2018; Poole et al., 2008). Maximal aerobic capacity declines with age (Garber et al., 2011) and is seldom observed in people with cardiovascular or pulmonary disease (Arena et al., 2007). When VO_{2max} fails to occurs, Peak Volume of O_2 (VO_{2peak}) is used therefore, commonly characterizes elderly's CRF (ACSM, 2018; Arena et al., 2007).

In line with successful aging, research has been devoted at clarifying the protective role and the effects of PA and PE in cognition and the brain. Cross-sectional investigations suggested that, independently of subjective (Benedict et al., 2013) or objective assessment of PA (Barnes et al., 2008; Brown et al., 2012; Buchman et al., 2008), physical active individuals tended to exhibit better memory and EF. Prospective studies (Hamer et al., 2018; Hayes et al., 2016; Loprinzi et al., 2019; Weuve et al., 2004; Yaffe et al., 2009; Zhu et al., 2017), reviews and metanalysis (Bherer et al., 2013; Chodzko-Azjko et al., 2009; Erickson et al., 2015) also support the assumption that PA is related to cognitive brain health.

The optimal intensity of PA to have cognitive benefits is not consensual. LPA (Stubbs et al., 2017; Umegaki et al., 2018), leisure-time PA (Barreto et al., 2018; Willey et al., 2016) and MVPA (Angevaren et al., 2007; Kerr et al., 2013) have all been associated with improved cognitive function or protective of cognitive decline, separately. Simultaneously, all-levels of PA have been related to cognition (Sofi et al., 2011), in a U-shape dose-response with MVPA as the optimal level (Loprinzi et al., 2018).

The exact cognitive benefits that may overcome with PA and the exact mechanism(s) underlying PA benefits are also unclear. One of the proposed mechanisms was CRF hypothesis, firstly proposed by Dustman et al., (1984). Aerobic training would be responsible for improvements in CRF, namely VO_{2max}, and such improvements would enhance cerebral metabolic activity; improve cerebral blood flow; increase perfusion and oxygenation of brain tissue and, consequently, improve neuropsychological function (Agbangla et al., 2019; Dustman et al., 1984). Later, Kramer et al., (1999) added that CRF would be responsible for changes in metabolic and neurochemical functions and consequently improve executive control processes. Cross-sectional investigations found a positive association between CRF and cognitive functions, independent of PA (Farrell et al., 2018; Freudenberger et al., 2016; Voss et al., 2016), exercise and sedentary behavior (Edwards & Loprinzi, 2017) or obesity (Boidin et al., 2020). Majority of evidence focused on memory and EF (or respective brain areas) or global cognition. According to CRF hypothesis, only interventions that reported VO_{2max} improvements would report cognitive improvements (Dustman et al., 1984; Kramer et al., 1999). Indeed, aerobic interventions have reported cognitive improvements (Billinger et al., 2016), indices of brain health (Colcombe et al., 2006; Weinstein et al., 2013) or both (Erickson et al., 2011; Kleinloog et al., 2019; Weinstein et al., 2013). Finally, reviewed findings regarding aerobic training (Smith et al., 2010) and aerobic fitness (Colcombe & Kramer, 2003; Erickson et al., 2015; Rigdon & Loprinzi, 2019), further support the impact of CRF in cognitive functions and brain structure.

With extensive review of PA and PE benefits in cognition and in the brain (Bherer et al., 2013; Chodzko-Azjko et al., 2009; Etnier et al., 2019; Gomes-Osman et al., 2018; Hillman et al., 2008; Kramer & Colcombe, 2018; Ploughman, 2008), PE interventions disseminated in order to answer one major question: what is the optimal program to optimize cognitive benefits? Besides frequency, intensity and duration, different interventions tried to gather information regarding different PE modalities, mainly aerobic and resistance exercise trainings. The first, defines exercises in which the body's large muscles move in a rhythmic manner for sustained periods and are responsible for improving CRF. Additional benefits are cardiovascular function; metabolic function and body composition (in overweight older adults seems to reduce total body fat with no effect on fat-free mass). Resistance training causes muscles to work or hold against an applied force or weight and improves muscle strength, quality and endurance and body composition (improving fat-free mass and decrease total fat mass from 1.6% to 3.4%). Both modalities seem to improve bone health and decrease the risk for clinical depression and anxiety (Chodzko-Azjko et al., 2009).

Simultaneously, there is evidence of a link between body composition and cognition. Several markers for a prodromal manifestation/risk factor for cognitive disfunction or dementia have been identified. Such as high (e.g. Gorospe & Dave, 2007; Gustafson et al., 2003) or low BMI (e.g. Arnoldussen et al., 2018; Nourhashémi et al., 2003), with lower BMI as a stronger risk factor (Cereda et al., 2007; Deschamps et al., 2002; Luchsinger et al., 2007); unintended weight loss (Barrett-Connor et al., 1996; Jimenez et al., 2017; Luchsinger et al., 2007; Stewart et al., 2005); accelerated rate of weight loss (Alhurani et al., 2016; Johnson et al., 2006) or of BMI decline (Wagner et al., 2018), from midlife to late-life.

BMI does not provide information about body composition and distribution of body fat, particularly in elderly (Luchsinger et al., 2007). Distribution of body fat seems relevant given the possible differential pattern of adiposity in cognition, according to age and regional distribution. In midlife, a loss of waist circumference or BMI were both associated with higher cognitive performance. In late-life, loss of waist circumference or BMI were associated with lower cognitive performance. Loss, stable and gain in BMI, in this order, were associated with decreased cognitive performance in midlife and with increased cognitive performance in late life (N. West et al., 2017). Moreover, vascular, inflammatory and metabolic, factors related to dementia seem more associated with central adiposity (Gustafson, 2006; Luchsinger et al., 2007). Contrarily, there is evidence for a major role of gynoid fat in cognition, in healthy elderly (Forte et al., 2017) and this link need to be clarified.

With evidence of differential physical effects and a link between body composition and cognition, different cognitive benefits according to exercise modalities were investigated. Resistance training interventions propose a link with EF (Li et al., 2018; Liu-Ambrose et al., 2010). Further investigation compared aerobic and resistance training either separately or combined – multicomponent exercise training (MCT). Smith et al., (2010) reported effects on attention, processing speed, memory and EF by aerobic training while MCT reported effects in working memory. Combined interventions improved attention, processing speed and working memory to a greater extent than aerobic training by itself. Voss et al., (2019) found a similar effect for MCT in memory, underlying that resistance training could boost but not replace, aerobic exercise effects on memory. When comparing the effects of aerobic, resistance and tai-chi (combined) interventions, aerobic exercise had contradictory findings, with only EFs being reliably improved. Whereas resistance training seemed to significantly improve reasoning and tai-chi to affect positively attention, processing speed and working memory (Kelly et al., 2014).

Ultimately, the hypothesis that MCT would be most beneficial to promote cognitive function and physical fitness in elderly was proposed and tested by randomized control trials (RCT), comparing aerobic and resistance training separately or combined. Majority of interventions focused on clinical samples and presented mixed results. A four-year RCT comparing aerobic, resistance or MCT failed to improve VO_{2max} but it still predicted lower incidence of impaired memory (Komulainen et al., 2010). Conversely, aerobic interventions have demonstrated capable of improving VO_{2max}, attention and abstract reasoning while resistance training improved praxis (Iuliano et al., 2015). Short-term MCTs have reported cognitive improvements in elderly's EFs - working memory and processing speed, and episodic memory (Bherer et al., 2019; Nouchi et al., 2014). Six-month MCT interventions either with cognitively health elderly in a nursing home (Arrieta et al., 2020) or with Portuguese Alzheimer's disease elderly (Sampaio et al., 2019), point out that MCT is, at least, effective in preserve cognitive abilities of these populations. The later also added evidence regarding physical fitness benefits (reduction in waist circumference, increased aerobic fitness) of MCT. Moderately frail obese older adults with a MCT (aerobic, resistance and balance) improved overall physical fitness, namely, (1)decreased fat mass; (2)increased fat-free mass and appendicular lean body mass; (3)increased peak aerobic capacity by approximately 15%; (4)increased endurance and muscle mass and strength (Villareal et al., 2011). For healthy elderly, resistance exercise did not interfere in elderly's cardiovascular function improvements while still improving elderly's strength, in a MCT (Burich et al., 2015). Contrarily, one MCT showed no effects in cognitive function (Ansai & Rebelatto, 2015) or CRF while reporting differences in total fat percentage (Nielsen et al., 2019). In sum, while MCT seems promising in improving elderly's cognition and physical fitness more evidence is necessary given the non-unanimous previous findings.

Discrepant evidence regarding MCT benefits urge the need of interventional studies to address the possible protective effect of PE in cognition, principally in cognitively healthy elderly. Evidence of the association between cognition and physical fitness is still unclear. Both are relevant to inform and adequate recommendations of PA (e.g. intensity, frequency, duration, type…) to the needs of each population and design the optimal program of PE according to them, promoting successful aging. Furthermore, interventions in Portuguese population are scarce. Current study aims at clarifying cognitive, emotional and physical fitness effects (aerobic fitness and body composition), of a MCT intervention in community-dwelling elderly and compare them with an active control group. Moreover, it aims at exploring the association between cognitive function and physical fitness. We hypothesize that after MCT, intervention group will present improved neurocognitive function, decreased emotional symptoms, improved aerobic capacity (VO_{2peak}), increased lean mass percentage and decreased body fat percentage, compared to control group. Additionally, we hypothesize that cognitive functions are associated with body composition and positively associated with VO_{2peak}.

Methods

Experimental Design

To assess the differential effect of MCT in cognitive function, body anthropometry and physical fitness, a double-blind quasi-experimental intervention was conducted. Current study was conducted within the project "*Mais Ativos, Mais Vividos*" with Faculty of Sports of Porto University (FADEUP) and University of Minho. Ethics Subcommission of Life and Health Sciences (SECVS 120/2016) approved all methods and procedures implemented.

Participants

Participants were community-dwelling older adults recruited to a PE program ("*Mais Ativos, Mais Vividos*") in FADEUP, through community advertisements and personal invitation, in the North of Portugal. Group allocation was done by a coordinator sports teacher according to registration order. Intervention group (MCG) was constituted with participants from the control group (CG) of the previous year or participants that registered for the first time if there were remain vacates. Otherwise, participants in first registration were allocated to CG which is stablished as an adaptation year. Attenders of "*Mais Ativos, Mais Vividos*" were invited to fill initial screening questionnaire, including sociodemographic characteristics and medical history. Data collection ranged from September 2016 to October 2019, with participants recruited in three different year-classes: 2016/2017, 2017/2018 and 2018/2019. Inclusion criteria for eligibility were: age above 60 years; being able to perform daily living activities independently; have a normal or corrected-to-normal vision; psychiatric medication (antidepressant or anxiolytic) without alterations during the program and attendance of the MCT>50%. Exclusion criteria were Body Mass Index (BMI)>40; prior history of neurodegenerative disorders, head injury, stroke, epilepsy; neurological or psychiatric disorder; clinical anxiety or major depressive disorder; cardiovascular or respiratory diseases, motor problems or other contraindications for CRF evaluation; presence of a visual, auditory or language impairment that could interfere the understanding of instructions or test completion; anticonvulsants medication and alcohol or drug abuse.

A total of 54 participants were screened to participate in the investigation. Final sample included 19 participants, eight in CG and 11 in MCG (see Figure 1; Table 3). Participants excluded in initial screening presented post-traumatic stress disorder (n=1), Major Depressive

Disorder (n=5), age>80yrs (n=6), BMI>40 (n=1), cardiovascular accident (n=1), cardiovascular diseases (n=3) and a knee prosthetics (n=1). For health-related reasons, one participant of MCG was not assed for anthropometry and only 12 were assessed for CRF (five from CG).

Intervention Group: Multicomponent Training Exercise (MCG)

Intervention group was provided with a multicomponent training program composed by aerobic, strength, stretching and balance exercises. Sessions of exercise lasted, approximately, 50 minutes and included: (1)10-minute warm-up, with slow walk, calisthenics and stretching exercises; (2)20-minute aerobic group class; (3)main muscle groups strength exercises performed in a circuit; (4)balance/coordination exercises, (5)10 minutes cool-down with respiratory and flexibility exercises. Heart rate (HR) was monitored (Polar Team System, Finland) and Rating of perceived exertion (RPE) was recorded on a 10-point scale at the end of each exercise session.

Control Group: Training Exercise (CG)

CG performed a weekly exercise session with a similar but less intense exercise protocol.

Materials/Instruments

Physical Activity

Accelerometry constitutes an objective way to determine intensity and duration of PA (Erickson et al., 2015; Troiano et al., 2008). The quantity and intensity of daily SED and PA may be obtained through the classification of activity counts accumulated in a specific time interval with pre-determined cut-points (intensity thresholds). Although accelerations can be detected in three axes (Migueles et al., 2017), current analysis focused exclusively in the vertical.

Weekly Percentage of PA Levels. Participants were instructed to use the accelerometer (Actigraph GT3X, Pensacola, Florida) for seven consecutive days at baseline (TO) and post-intervention (T1) in all walking hours, except while sleep, bathing or water-based activities and to do their daily routine and normal physical activities. Researchers showed how to place the monitor of the accelerometer with its adjustable waistband: over the right hip close to the iliac crest. In a diary, participants registered waking and bedtime, moments of non-wear and why (e.g. shower or swimming) and description and time performing any PA.

Accelerometer was programmed to record data as counts per minute (cpm) at a frequency of 30 Hz and 1 s length epochs (specific time intervals). Accelerometer data were downloaded, reviewed and analyzed with ActiLife v6.0 software (Pensacola, Florida) and integrated into 60-second epochs. Non-wear time was removed from the analysis and was previously determined as 60 consecutive minutes of zero counts, during which no activity was recorded. For a daily record to be considered as a valid day (i.e., the number of hours per day) was required at least nine hours/day of wear time and participants with less than four valid-days (three week-days and one weekend-day) were excluded (Choi et al., 2011; Migueles et al., 2017; Schmidt et al., 2020). If wearing-criteria were not met, participants were asked to re-do the wearing procedure (n=1).

Percentage of time spent in each PA level during the week was categorized by SED (0-99 cpm); LPA (100-2019 cpm) and MVPA (≥2020 cpm) (Troiano et al., 2008). Weekly percentage in each PA level was averaged according to percentage of time spent in each PA level per day and available recorded days.

PA Levels of Exercise Programs. During exercise sessions some participants were asked to use the accelerometer (GT9X). Percentage of time spend in each PA level was calculated to assess PE programs effectiveness at improving participants' PA. Levels were categorized as SED (0-199 cpm); LPA (200-2751 cpm) and MVPA (≥2752 cpm) (Aguilar-Farías et al., 2014; Migueles et al., 2017; Santos-Lozano et al., 2013).

Physical Fitness

Anthropometry. Participants were submitted to a Dual Energy X-ray Absorptiometry (DEXA) protocol after height and weight measurement, assessing Bone Mineral Density (BMD) and body composition (fat mass percentage, lean mass percentage, android-gynoid ratio and fat distribution).

Cardiorespiratory Fitness. CRF assessment was conducted by the Modified Bruce protocol on a treadmill (Quasar, h/p/cosmos, Germany) with a standard open-circuit spirometer technique (Oxycon Pro Metabolic Cart, Jaeger, Carefusion, Germany) at Centro de Investigação em Actividade Física, Saúde e Lazer (CIAFEL). Participants were asked not to engage in intense PA for at least 24 hours before the test.

Participants started with a warm-up period on the motor-driven treadmill to familiarization. Modified Bruce protocol (see Table 1) is a multistage protocol each stage lasting for three minutes to ensure a steady stage of HR response. During the exercise test, strong verbal encouragement was given and the modified Borg Scale (Borg, 1998) assessed self-perceived exertion. Participants' HR was monitored, oxygen uptake (VO_2), carbon dioxide production (VCO_2) and respiratory exchange ratio (RER) (i.e., exchange ratio between metabolic carbon dioxide and volume of oxygen consumed, calculated dividing VCO_2 by VO_2) were collected. Test continued until exhaustion at the maximal volitional work rate unless there were medical indications for termination, which was not the case (ACSM, 2018; Borg, 1998). At the end, there was a post-exercise cool-down period.

Maximal effort of participants was defined as ACSM guidelines (2018): a plateau in VO_2 and failure of HR to increase both with further increases in workload, at the same time that RER>1.10 and maximal heart rate (HRmax) was ≥85% of the age-predicted HRmax (calculated as 220-age). Validity of secondary criteria to determine VO_{2max} may be questioned (Poole et al., 2008). Majority of participants failed to fulfil them. CRF was defined as VO_{2peak} relative to bodyweight (ml · kg-1 · min-1) and reported as the 30-seconds mean VO_2 of the highest performance level achieved by each participant.

Table 1

Description of the Modified Bruce Protocol

Stage	Speed (km/hour)	Grade (%)
1	2.7	0
2	2.7	5
3	2.7	10
4	4.0	12
5	5.4	14
6	6.7	16
7	8.0	18
8	8.8	20
9	9.6	22

Note. Based on (ACSM 2018).

Cognitive Function

To assess the effect of MCT in emotional status and neurocognitive function, participants were submitted to a psychological assessment protocol (see Table 2). It included Geriatric Anxiety Inventory (GAI) (Ribeiro et al., 2011), with scores >8/9 representing severe anxiety symptoms and Geriatric Depression Scale (GDS) (Pocinho et al., 2009), with scores >11 indicating depressive disorder.

Table 2

Neuropsychological Assessment Protocol According to Neurocognitive Function

Psychological Function	Test(s)	Description
Global cognition	Montreal Cognitive Assessment (MOCA) (Freitas et al., 2011; Nasreddine et al., 2005)	Is a screening for cognitive decline and assesses EF; visuospatial abilities; short-term memory; language; attention; concentration and working memory; temporal and spatial orientation. Maximal score is 30 and has different cut-off scores according to age and education. Only raw score was analyzed.
Language	Verbal Fluency Tests: Phonemic Fluency (M; P; R) and Semantic Fluency (animals) (Cavaco et al., 2013a).	Assesses EF, processing speed and language production. Participants are asked to orally generate as many words as they can beginning in M, P and R or animals for one minute. There are scores according to age and education, but raw scores were analyzed.
Processing Speed/ Attention	Trail Making Test – part A (Cavaco et al., 2013b)	Assesses attention; visual scanning; speed of eye-hand coordination; information processing and motor speed skills. Participant is asked to draw consecutive lines to connect 25 encircled numbers. Direct score of time to complete was analyzed.
	Symbol Search (Wechsler, 2008)	Assesses EF, namely, processing speed.
Executive functions	Trail Making Test – part B (Cavaco et al., 2013b)	Assesses mental flexibility or task-switching; reflects working memory function. Participant is asked to connect encircled numbers and letters. Direct score of time to complete was analyzed.
	Digit Span Backwards (Wechsler, 2008)	Assesses working memory. Participants are read a sequence of numbers and are asked to repeat them in the reverse order.
Memory	Digit Span Forwards (Wechsler, 2008)	Assess short-term memory. Participants are read a sequence of numbers and asked to repeat them in order.
	Logic Memory I and II (Wechsler, 2008)	Assesses auditory memory, both short-term (I) and long-term (II). Participants are asked to recall stories they heard with as many details as possible.
	Verbal Paired Associates I and II (Wechsler, 2008)	Assesses verbal memory, both sort-term (I) and long-term (II). Participants are read unrelated paired words and asked to recall them.
	Visual Reproduction I and II (Wechsler, 2008)	Assesses visual memory, both short-term (I) and long-term (II). Five different geometric drawings are presented to the participants for 10 seconds and then they are asked to reproduce them by memory. Total sum of raw scores (0-104) were analyzed.

Procedure

Attenders of "*Mais Ativos, Mais Vividos"* were invited to fill initial screening. Eligible candidates were invited to a clarification session, explaining aims and procedures of the project. It aimed at examining cognitive and brain changes after an exercise intervention. Candidates with interest, were provided written consent and individual assessment sessions in the following month were scheduled.

There were two evaluations, at baseline (T0) and after the 33-week intervention (T1). Global evaluations included all previous measures. Cognitive assessment was conducted by a trained psychologist. Physical fitness assessment was conducted by a trained sports technician. Following each assessment, participants used the accelerometer for seven consecutive days.

Both exercise programs were defined *a priori* by a coordinator sports teacher and were conducted by him or his interns.

Data Analysis

Analysis were performed in SPSS v26 with a level of significance of $p < .05$. Missing values were treated as pairwise, when that option was available.

All data were first tested for parametric assumptions with Shapiro-Wilk test and homogeneity of variances. First analysis aimed at evaluating possible initial between-group differences, consisting in a two-independent samples t-test or the non-parametric equivalent, Mann-Whitney.

To evaluate the effects of the MCT in neurocognitive function, emotional status and physical fitness, a Repeated Measures Analysis of Covariance (RM-ANCOVA) was conducted for each cognitive test or measure separately. Within-subject factor was time (T0 and T1) and between-group factor was group (CG vs MCG). Sex, age, years of education and psychiatric medication were included as covariates. In significative interactions, Post-hoc Bonferroni analysis were conducted. Partial Eta Squared (η^2) was reported as an index of effect size. For non-parametric data, the equivalent Kruskal-Wallis for k-independent samples (CG T0; CG T1; MCG T0 and MCG T1) was conducted, without covariates.

Results

Participants enrolled in the study are represented in Figure 1. At T0, MCG had significantly higher frequency of hypertension diagnosis comparing to CG, $U = 19.00$, $z = -2.41$, $p = .041$. No more significant differences were found in sociodemographic or clinical characteristics of participants, neurocognitive functioning, emotional symptomatology or physical fitness (see Table 3).

Exercise attendance was controlled, being MCG (*M* = 72.21; *SD* = 11.66) mean adherence superior than CG (*M* = 62.20; *SD* = 23.45), however no significant difference was found, t(17) = -1.23, *p* = .235, 95% CI=]-27.18; 7.14[.

Criteria for reaching a maximal VO_2 test (e.g. RER>1.10) (ACSM, 2018) were reviewed. At T0 (n=18), only 33.33% of participants fulfilled them. Thereby, our data analyzed the submaximal VO_2 (VO_{2peak}).

PA Levels Analysis of the Exercise Programs

PA levels analysis revealed that percentage of time in MVPA during exercise session was significantly higher for MCG (*M* = 25.00; *SD* = 4.23) compared to CG (*M* = 13.05; *SD* = 7.10), t(15)= -4.36; *p* = .001, 95% CI=]-17.79; -6.11[. Percentage of time in LPA was slightly lower for MCG *(M* = 61.67; *SD* = 5.15) compared to CG (*M* = 63.30; *SD* = 6.81), however no significant difference was found, t(15)= 0.56, *p* = .581, 95% CI=]-4.53; 7.80[. Percentage of time in SED was significantly lower for MCG (*M* = 13.33; *SD* = 7.74) compared to CG (*M* = 23.64; *SD* = 6.50), t(15)= 2.88, *p* = .011, 95% CI=]2.68; 17.95[.

Figure 1

Flow Chart of Participants

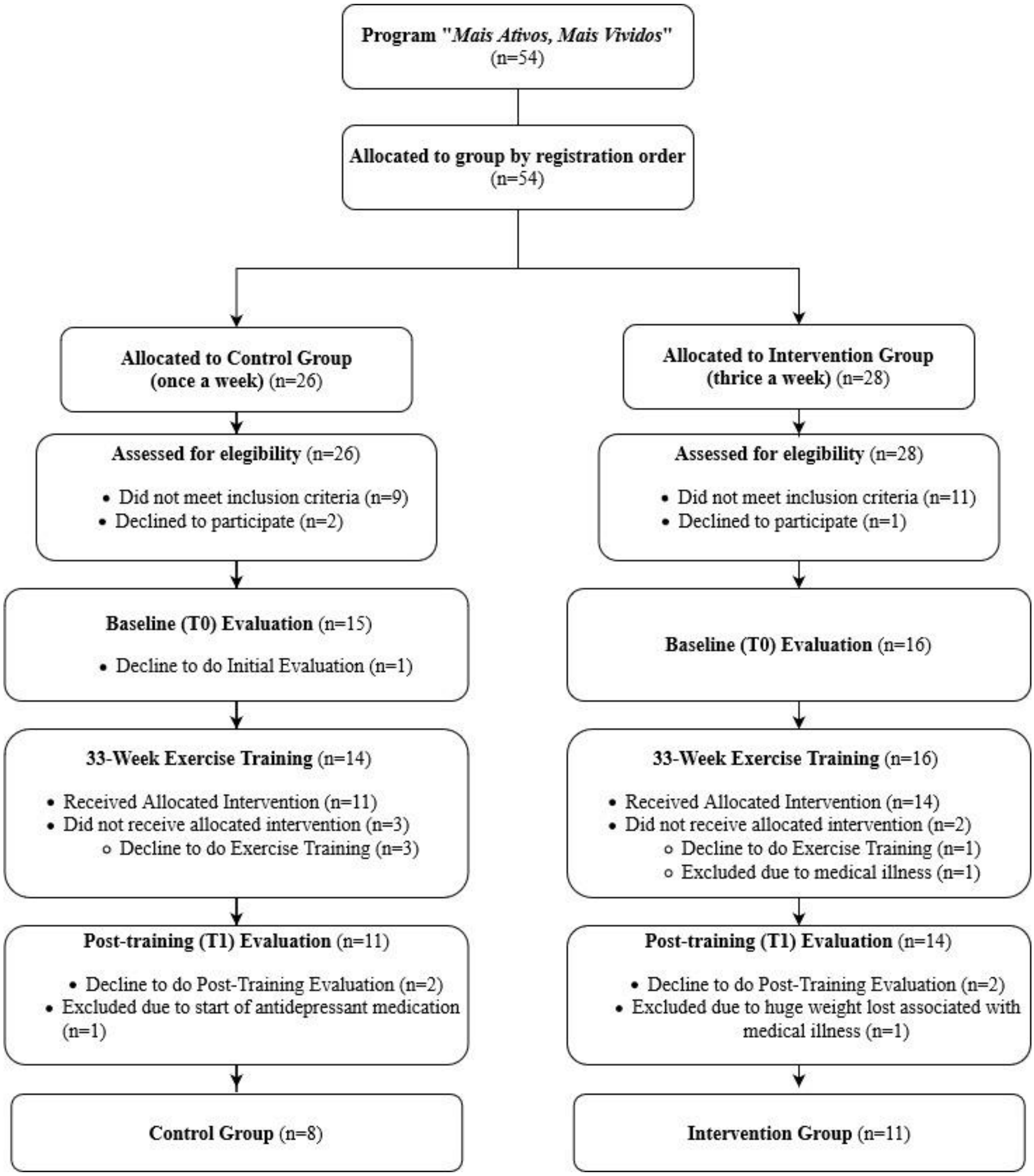


Table 3

Demographic and Clinical Profile of Participants at Baseline (T0) and Between-Group Differences

Characteristics	Total (n=19)	MCG (n=11)	CG (n=9)	*p*
Age (years) (M, SD)	68.00 (3.30)	68.82 (3.95)	66.88 (1.81)	.272[b]
Feminine, n (%)	13 (68.42)	6 (54.55)	7 (87.50)	.238[b]
Education (years) (M, SD)	11.47 (4.11)	12.09 (3.91)	10.63 (4.50)	.459[a]
Vocabulary test score (M, SD)	44.26 (8.74)	46.55 (9.88)	41.13 (6.13)	.062[b]
Diagnoses and medical conditions, n (%)				
Hypertension	11 (57.90)	9 (81.80)	2 (25.00)	.041[b*]
Cholesterol	5 (26.30)	3 (27.30)	2 (25.00)	.968[b]
Bone problems	3 (15.80)	1 (9.09)	2 (25.00)	.600[b]
Prostate problems	1 (5.30)	0	1 (12.50)	.657[b]
Vesicle	1 (5.30)	0	1 (12.50)	.657[b]
Meniere's syndrome	1 (5.30)	0	1 (12.50)	.657[b]
Thyroid problems	2 (10.50)	0	2 (25.00)	.395[b]
Sleep apnea	1 (5.30)	1 (9.09)	0	.778[b]
Prescribed medication, n (%)				
Antihypertensives	12 (63.20)	9 (81.80)	3 (37.50)	.109[b]
Statins	5 (26.30)	3 (27.30)	2 (25.00)	.968[b]
Antiasthmatic	1 (5.30)	1 (9.09)	0	.778[b]
Psychiatric medication (antidepressant and/or anxiolytic)	4 (21.10)	2 (18.20)	2 (25.00)	.840[b]
Physical Activity Levels (%)				
Sedentary Time (%)	64.51 (6.30)	65.00 (6.44)	63.84 (6.48)	.702[a]
LPA Time (%)	29.43 (6.62)	28.94 (6.65)	30.09 (6.98)	.720[a]
MVPA Time (%)	6.06 (2.76)	6.06 (3.21)	6.07 (2.21)	.990[a]
Anthropometry (M, SD)				
BDM (g/cm^2)	1.03 (0.11)	1.03 (0.09)	1.03 (.13)	.492[b]
BMI (kg/m^2)	28.90 (3.02)	28.60 (3.38)	29.31 (2.59)	.625[a]
Android-Gynoid Ratio	1.08 (0.15)	1.13 (0.16)	1.03 (0.12)	.141[a]
Total body fat percentage (%)	39.50 (7.28)	37.45 (7.46)	42.30 (6.41)	.157[a]
Lean mass percentage (%)	57.78 (7.05)	59.74 (5.96)	55.08 (7.38)	.160[a]

Characteristics	Total (n=19)	MCG (n=11)	CG (n=9)	*p*
Lean mass per height square Index (kg/m^2)	16.93 (2.72)	17.52 (3.31)	16.14 (1.45)	.600[b]
Android fat percentage (%)	40.86 (6.64)	40.00 (5.14)	42.05 (8.53)	.522[a]
Gynoid fat percentage (%)	37.97 (7.94)	36.29 (7.69)	40.28 (8.18)	.238[b]
VO_{2peak} mL.Kg^{-1}.min^{-1} (M, SD)	27.51 (4.85)	28.66 (2.10)	26.21 (6.72)	.423[b]
Psychological outcomes (M, SD)				
GAI	3.42 (3.85)	3.36 (3.85)	3.50 (4.11)	.717[b]
GDS	3.21 (2.86)	3.64 (1.04)	2.63 (1.85)	.717[b]
TMT-A (time)	41.83 (22.23)	42.39 (26.65)	41.06 (15.98)	.778[b]
TMT-B (time)	148.47 (69.56)	138.36 (79.82)	162.38 (54.39)	.310[b]
Symbol search	16.68 (11.37)	16.09 (13.13)	17.50 (9.21)	.798[a]
MOCA	24.37 (3.42)	24.73 (3.98)	23.88 (2.65)	.606[b]
Phonemic fluency	33.00 (10.32)	32.55 (9.83)	33.63 (11.61)	.829[a]
Semantic fluency	16.32 (4.18)	15.45 (4.57)	17.50 (3.51)	.305[a]
Digit span forwards	8.42 (2.22)	8.55 (2.46)	8.25 (1.98)	.784[a]
Digit span backwards	5.79 (1.81)	6.09 (1.92)	5.38 (1.69)	.411[a]
Verbal paired associates I	13.83 (7.68)	13.70 (8.10)	14.00 (7.67)	.300[a]
Verbal paired associates II	4.70 (2.28)	4.91 (1.51)	4.63 (3.16)	.904[b]
Logic memory I	37.16 (9.84)	37.18 (12.47)	37.13 (5.17)	.778[b]
Logic memory II	24.37 (6.68)	26.18 (7.08)	21.88 (5.54)	.171[a]
Visual reproduction I	68.83 (20.17)	70.73 (23.92)	65.86 (13.50)	.632[a]
Visual reproduction II	54.89 (21.79)	28.66 (2.10)	48.38 (60.37)	.557[a]

[a]: two-independent sample Student's t-test. [b]: Mann Whitney-U test.

* $p < .05$.

Effects of MCT Exercise Intervention

Physical Fitness Effects

Anthropometry. No significant main effects, interactions or between-group differences for anthropometric outcomes were found ($p > .05$) (see Table 4). A slightly increase in lean mass % ($p = .777$) and decrease in total body fat % ($p = .850$) from T0 to T1 was observed, for both groups. MCG slightly decreased android and gynoid fat percentages while CG slightly increased them ($p = .112$; $p = .259$, respectively).

Cardiorespiratory Fitness. RM-ANCOVA was conducted for VO_{2peak} although assumption of homogeneity of variances was not met. A significant main effect of time was found, after controlling for participants' age and years of education, $F(1,6) = 20.43$, $p = .004$, partial $\eta^2 = .773$ (see Table 4.1).

A significant interaction between time and group was found for VO_{2peak} $F(1,6)=9.28$, $p = .023$, partial $\eta^2 = .607$. Post-hoc Bonferroni revealed that CRF for MCG at T1 was significantly lower compared to T0 ($p = .015$). The increase of VO_{2peak} observed from T0 to T1 in CG almost reached significance ($p = .092$).

Neurocognitive Effects

Neurocognitive effects after a 33-week intervention are represented in Table 4.

From T0 to T1, both groups significantly decreased their performance in semantic fluency with a significant main effect for time, $F(1,13) = 11.80$, $p = .004$, partial $\eta^2 = .476$ (see Table 4.1).

A significant interaction between time and group was found for digit span backwards (working memory), after controlling for age and psychiatric medication, $F(1,13) = 7.236$, $p = .019$, partial $\eta^2 = .358$. Post-hoc Bonferroni revealed a significant decrease in performance ($p = .036$) from T0 to T1 for MCG, without a significant increase ($p = .091$) in CG (see Table 4.1).

For the remaining neurocognitive functions, there were no significant main effects, interactions or between-group differences. CG tended to improve or, at least, maintain neurocognitive test performances. MCG followed the same tendency aside from auditory memory (logic memory I and II) that slightly decreased.

Emotional Status Effects

No between-group differences were found for anxious and depressive symptoms albeit scores in GAI and GDS decreased for both groups from T0 to T1 (see Table 4.2).

Table 4

Table 4.1

Means, Standard Deviations, and RM-ANCOVA for Neurocognitive Test Scores, Anthropometry and CRF

	MCG		CG		*p* (Group)	η2 (Group)	*p* (Time)	η2 (Time)	*p* (Interaction)	η2 (Interaction)
	T0 M(SD)	T1 M(SD)	T0 M(SD)	T1 M(SD)						
BMI (kg/m^2)	28.81 (3.49)	28.45 (3.27)	29.31 (2.59)	29.24 (2.86)	.756	.008	.846	.003	.871	.002
Android-gynoid ratio	1.15 (0.14)	1.15 (0.15)	1.03 (0.12)	1.05 (0.10)	.127	.183	.756	.008	.129	.181
Body fat %	36.80 (7.52)	35.49 (7.81)	42.30 (6.41)	42.24 (7.03)	.604	.023	.850	.003	.305	.087
Lean mass %	60.39 (7.44)	61.68 (7.67)	55.08 (5.96)	55.16 (6.58)	.586	.025	.777	.007	.292	.092
Android fat %	39.83 (5.38)	38.12 (5.25)	42.05 (8.53)	42.88 (8.83)	.240	.113	.483	.042	.112	.197
VO_{2peak} mL.Kg^{-1}.min^{-1}	28.66 (2.10)	28.29 (1.59)	26.21 (6.72)	28.24 (5.73)	.841	.007	.004*	.773	.023*	.607
MOCA	24.73 (3.98)	25.55 (3.27)	23.88 (2.64)	23.88 (2.59)	.494	.037	.711	.011	.372	.062
Phonemic fluency	32.55 (9.83)	35.18 (9.79)	33.63 (11.61)	37.00 (10.86)	.928	.001	.384	.059	.840	.003
Semantic fluency	15.45 (4.57)	14.73 (5.85)	17.50 (3.51)	16.25 (4.98)	.813	.004	.004*	.476	.145	.156
Digit span forward	8.55 (2.46)	9.09 (2.43)	8.25 (1.98)	9.25 (1.28)	.655	.016	.600	.022	.915	.001
Digit span backwards	6.09 (1.92)	5.09 (2.34)	5.38 (1.69)	6.25 (2.61)	.904	.001	.559	.027	.019*	.358
Verbal paired associates I	13.70 (8.10)	14.60 (6.40)	14.00 (7.67)	15.50 (7.11)	.734	.010	.272	.099	.865	.003

	MCG		CG		*p* (Group)	η2 (Group)	*p* (Time)	η2 (Time)	*p* (Interaction)	η2 (Interaction)
	T0 M(SD)	T1 M(SD)	T0 M(SD)	T1 M(SD)						
Logic memory II	26.18 (7.08)	25.91 (5.75)	21.88 (5.54)	22.38 (6.87)	.073	.226	.248	.101	.664	.015
Visual reproduction I	70.73 (23.92)	72.82 (22.72)	65.86 (13.50)	74.86 (10.51)	.428	.053	.525	.034	.793	.006
Visual reproduction II	57.70 (24.42)	65.30 (24.34)	51.38 (18.99)	59.75 (17.72)	.115	.194	.066	.254	.633	.020

Note. RM-ANCOVA: Repeated-Measures Analysis of Covariance for parametric outcomes; each test was conducted separately, T0 and T1 as within-subject factor and group as between-subject factor, controlling for sex, age, years of education and psychiatric medication.

*: $p < .05$

Table 4.2

Median and Kruskal-Wallis for k-Independent Samples for Neurocognitive and Emotional Test Scores, Anthropometry and CRF

	MCG		CG		*p*	H statistic
	T0 (Med)	T1 (Med)	T0 (Med)	T1 (Med)		
BMD (g/cm^2)	1.01	1.02	0.95	0.96	.740	1.256
Lean mass per height square (kg/m^2)	16.40	17.60	15.90	16.00	.556	2.081
Gynoid fat %	34.40	31.80	44.05	44.85	.259	4.023
TMT-A	38.40	37.00	37.75	34.00	.942	0.390
TMT-B	115.00	113.00	149.50	119.50	.312	3.571
Symbol search	14.00	28.00	18.50	21.00	.263	3.984
Verbal paired associates II	5.00	5.00	5.00	5.00	.851	0.793
Logic memory I	45.50	42.00	37.50	39.00	.680	1.511
GAI	3.18	2.00	3.00	2.00	.940	0.403
GDS	3.00	2.00	2.50	2.00	.898	0.592

Note. For non-parametric outcomes; MCG T0, MCG T1, CG T0 and CG T1 as independent variables.

*: p-value<0.05.

Neurocognitive Performance According to Physical Fitness

Global primary analysis did not report significant effects of MCT. Despite awareness that MCT partially replaced aerobic component by resistance training, the significant decrease of VO_{2peak} in MCG was unexpected. Participants may have reached different PA levels within exercise sessions, influencing possible cognitive and physical effects. Moreover, a wide inter and intra-individual variability was observed in neurocognitive test performance of all participants (see Figure 2). Thereby, we tested if variations in physical fitness would be associated with variations in neurocognitive test performance, aiming a personalized approach. Neurocognitive tests were selected to be representative of neurocognitive functions.

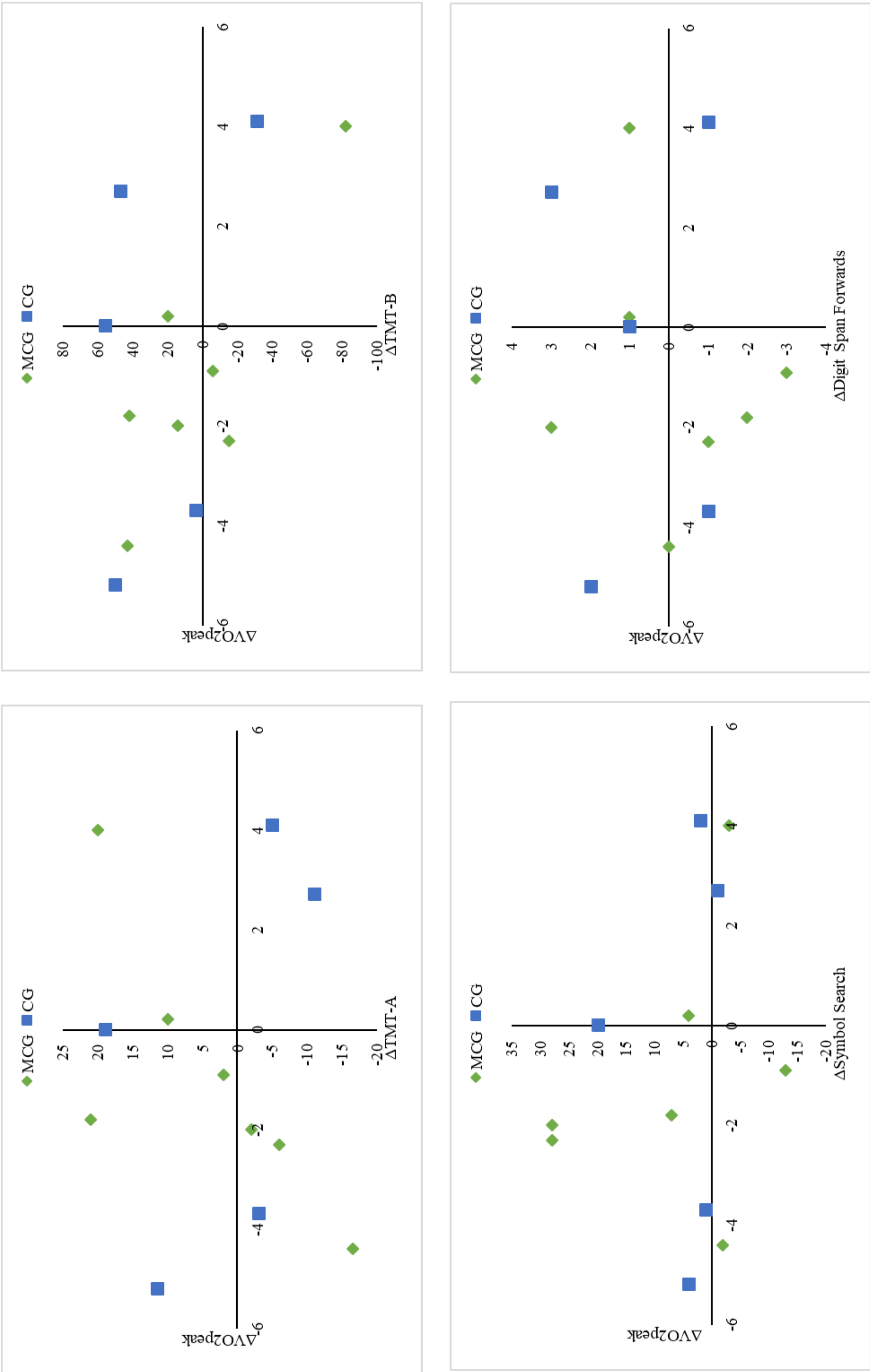
Variables were computed as deltas (Δ), representing its variation, by subtracting T0 test score from T1 score, or respective physical fitness variable (e.g.: ΔCRF=CRF T1 – CRF T0).

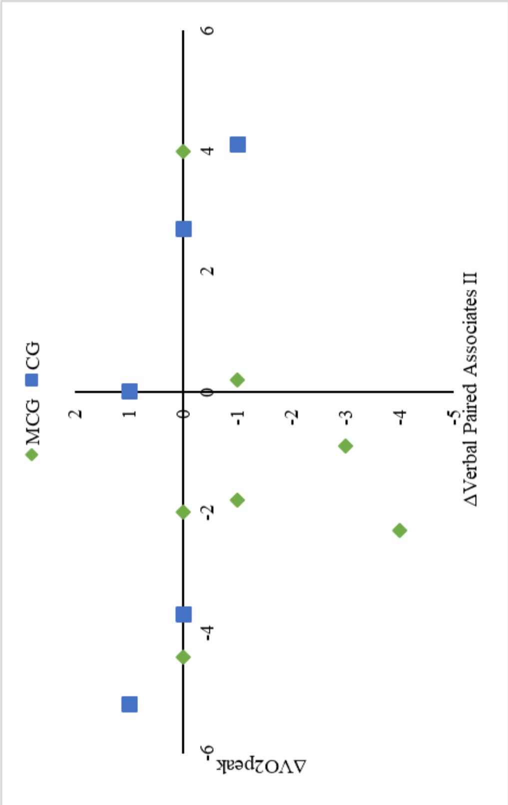
Pearson's Partial Correlation was run between Δphysical fitness and Δneurocognitive test scores with age, sex, years of education, Δtotal body fat percentage (Forte et al., 2017) and attendance of training as covariates. Attendance was included because CG attendance could be <50%. Kendall's tau-b bivariate correlation was run for non-parametric variables because it is more accurate for small sample sizes.

Figure 2

Figure 2.1.

Distribution of ΔVO_{2peak} and ΔNeurocognitive Test Scores




MCG
CG
ΔVerbal Paired Associates II
ΔVO2peak

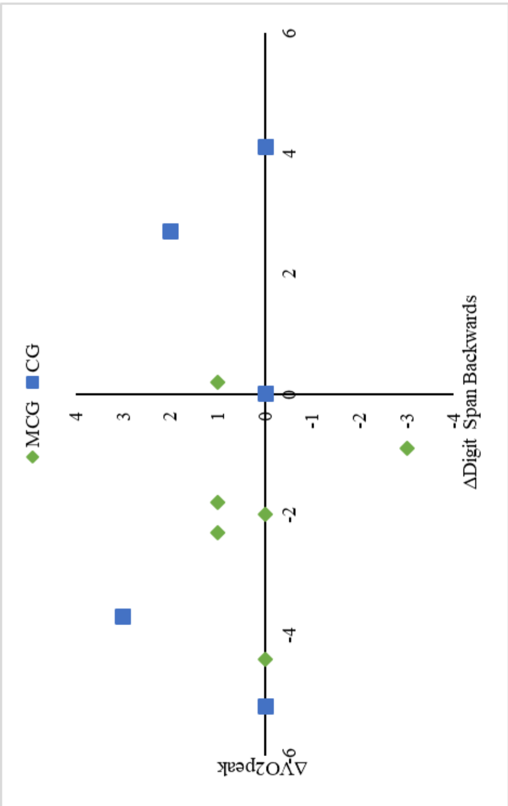
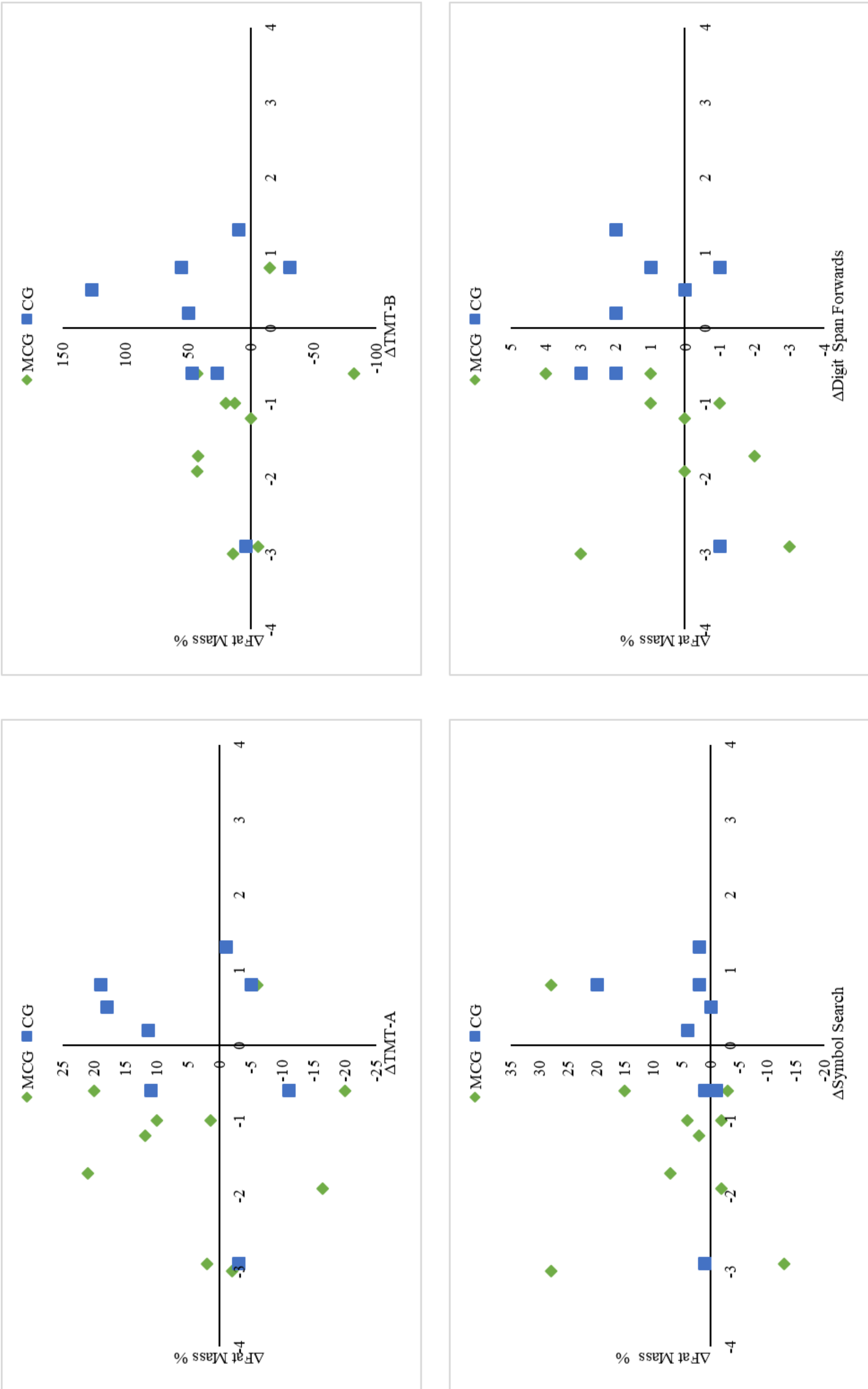
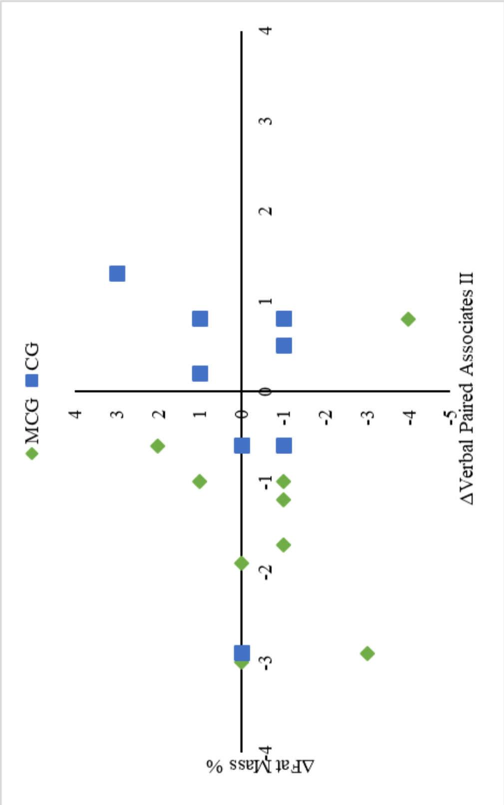

MCG
CG
ΔDigit Span Backwards
ΔVO2peak

Figure 2.2.

Distribution of ΔTotal Fat Mass % and ΔNeurocognitive Test Scores




MCG
CG
ΔVerbal Paired Associates II
ΔFat Mass %

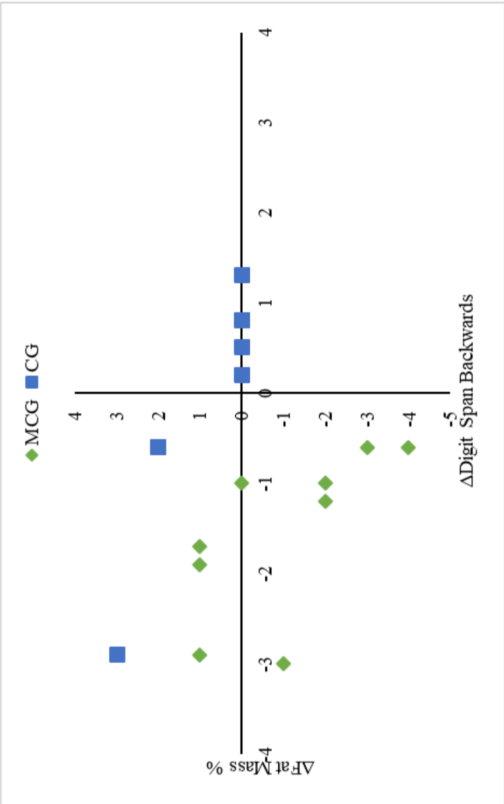
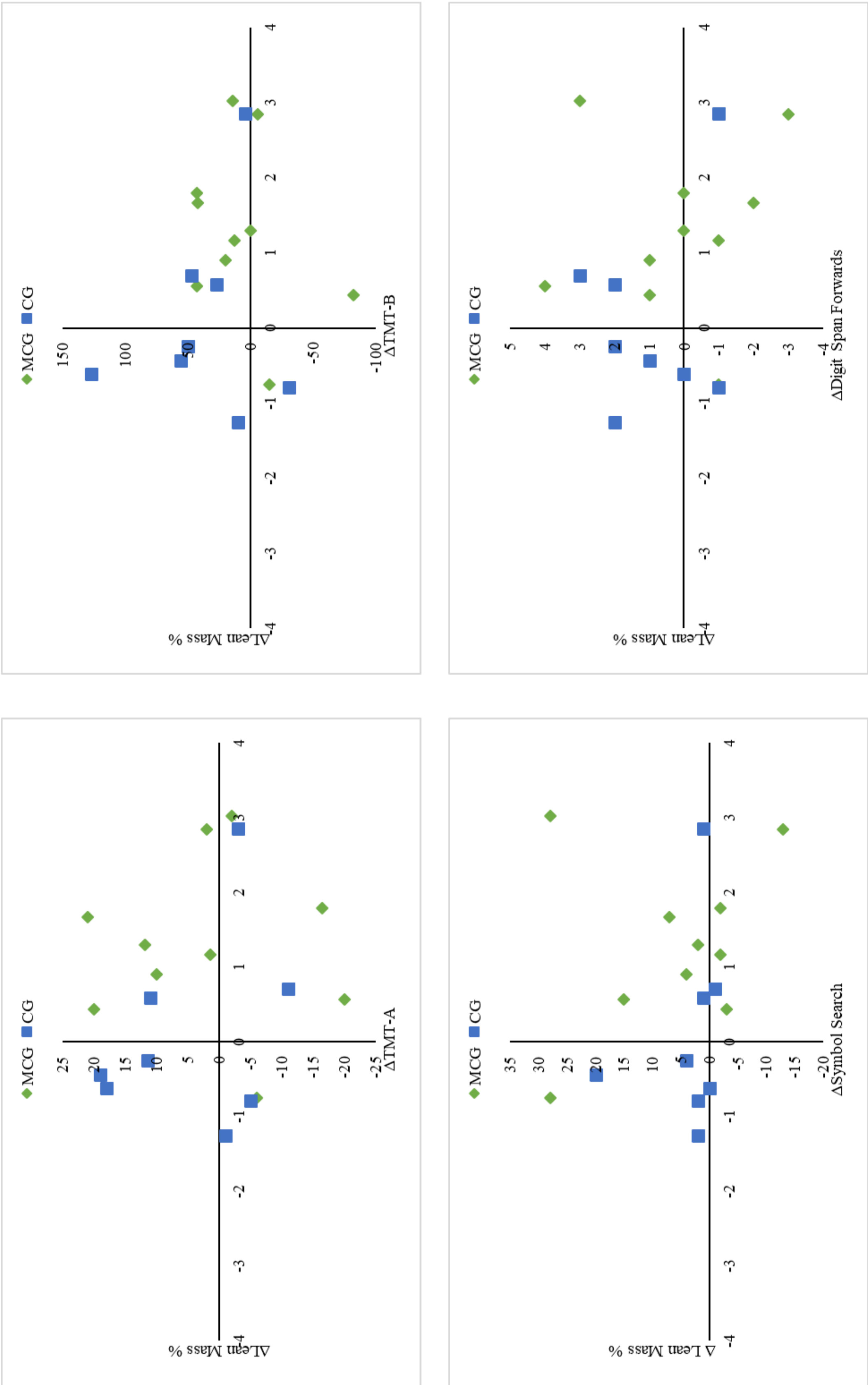
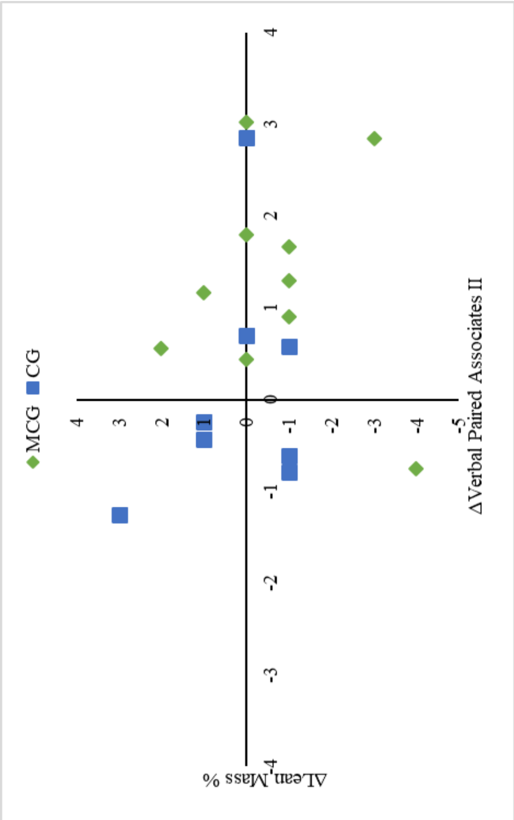
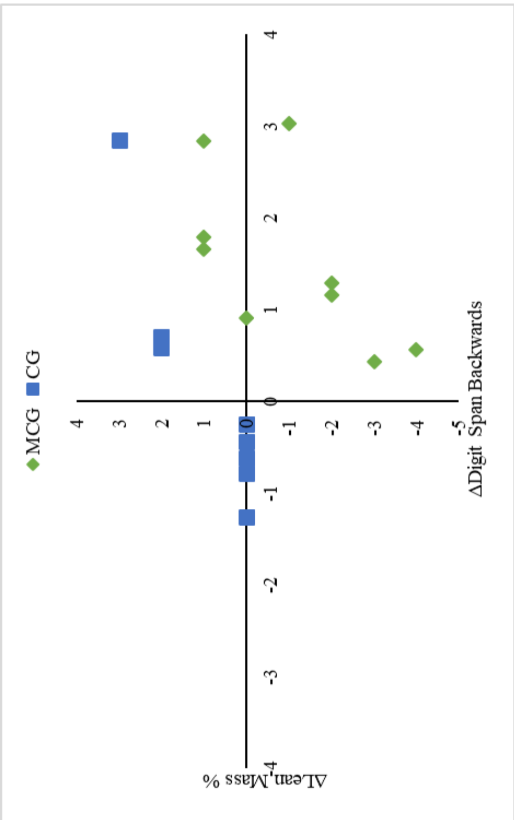

MCG
CG
ΔDigit Span Backwards
ΔFat Mass %

Figure 2.3.

Distribution of ΔLean Mass % and ΔNeurocognitive Test Scores







Note. MCG: multicomponent group. CG: control group.

Anthropometry

Sociodemographic and clinical characteristics of the 18 participants included in the association analysis with Δanthropometry are represented in Table 5. Δandroid fat % was significantly different between MCG (*M*=-1.71; *SD*=1.47) and CG (*M*=0.83; *SD*=1.61), t(16)= 3.49, p = .003, CI=]1.00;4.07[. Frequency of hypertension diagnosis was significantly higher for MCG compared to CG, U = 14.00, z = -2.73, p = .021. No more significant differences were found.

Associations between variations in physical fitness were found. A significant negative correlation between Δgynoid fat mass % and Δandroid-gynoid ratio (r = -.65, p = .023) was found. Δgynoid fat mass %, Δandroid-gynoid ratio and Δlean mass %, were significantly associated with ΔVO_{2peak} (r = -1.00, p < .001; r = 1.00, p < .001, r = .95, p = .003, respectively). Δandroid-gynoid ratio almost correlated positively with variations in short-term memory (Δdigit span forwards; r = .53, p = .078). Δgynoid fat mass % almost correlated positively with variations in processing speed/attention (Δsymbol search; t = .33, p = .062; see Table 7).

Cardiorespiratory Fitness

Twelve participants performed CFR assessment in both time points. Their sociodemographic and clinical characteristics are represented in Table 6. No significant between groups differences were found. 28.57% participants of MCG presented ΔVO_{2peak}>0.

ΔVO_{2peak} was positively associated with variations in short-term memory (r = 1.00, p < .001) and long-term memory (Δverbal paired associates; r = 1.00, p < .001; see Table 7).

Table 5

Demographic and Clinical Profile of Participants at T0 Included in Correlation Analysis Between Variations in Anthropometry and in Neurocognitive Function and Between-Group Differences

	Total (n=18)	MCG (n=10)	CG (n=8)	*p*
Age (years) (M, SD)	67.72 (3.16)	68.40 (3.89)	66.88 (1.81)	.408[b]
Education (years) (M, SD)	11.89 (3.80)	12.90 (3.00)	10.63 (4.50)	.083[b]
Feminine, n (%)	12 (66.67)	5 (50.00)	7 (87.50)	.203[b]
$VO_{2peak\ mL.Kg-1.min-1}$ (M, SD) at baseline	27.73 (4.92)	29.25 (1.19)	26.21 (6.72)	.442[b]
Diagnoses and medical conditions, n (%)				
Hypertension	11 (61.11)	9 (90.00)	2 (25.00)	.021[b*]
Cholesterol	4 (22.22)	2 (20.00)	2 (25.00)	.897[b]
Bone problems	3 (16.67)	1 (10.00)	2 (25.00)	.633[b]
Prostate problems	1 (5.56)	0	1 (12.50)	.696[b]
Vesicle	1 (5.56)	0	1 (12.50)	.696[b]
Meniere's syndrome	1 (5.56)	0	1 (12.50)	
Thyroid problems	2 (11.11)	0	2 (25.00)	.408[b]
Sleep apnea	1 (5.56)	1 (10.00)	0	.762[b]
Prescribed medication, n (%)				
Antihypertensives	12 (66.67)	9 (90.00)	3 (37.50)	.068[b]
Statins	5 (27.78)	3 (30.00)	2 (25.00)	.897[b]
Antiasthmatic	1 (5.56)	1 (10.00)	0	.762[b]
Psychiatric medication	3 (16.67)	1 (10.00)	2 (25.00)	.633[b]
ΔLean mass % (M, SD)	0.75 (1.32)	1.29 (1.13)	0.08 (1.29)	.051[a]
ΔAndroid fat mass % (M, SD)	-0.58 (1.97)	-1.71 (1.47)	0.83 (1.61)	.003[a*]
ΔGynoid fat mass % (M, SD)	-0.42 (1.68)	-0.89 (1.85)	0.18 (1.32)	.274[b]
ΔAndroid-gynoid ratio (M, SD)	0.01 (0.03)	-0.01 (0.02)	0.02 (0.04)	.124[a]
ΔTMT-A (M, SD)	3.40 (12.57)	2.18 (13.96)	4.94 (11.33)	.805[a]
ΔTMT-B (M, SD)	20.10 (43.19)	7.19 (37.54)	36.25 (46.70)	.117[a]
ΔSymbol search (M, SD)	5.17 (10.83)	6.40 (13.49)	3.63 (6.78)	897[b]
ΔDigit span forwards (M, SD)	0.56 (1.89)	0.20 (2.15)	1.00 (1.51)	.638[a]
ΔDigit span backwards (M, SD)	-0.11 (1.78)	-0.90 (1.79)	0.88 (1.25)	.083[b]
ΔVerbal paired associates II (M, SD)	-0.28 (1.64)	-0.70 (1.77)	0.25 (1.39)	.167[a]

[a]: two-independent sample Student t-test. [b]: Mann Whitney-U test.

[*] $p < .05$.

Table 6

Demographic and Clinical Profile of Participants at T0 Included in Correlation Analysis Between Variations in CRF and Variations in Neurocognitive Function and Between-Group Differences

	Total (n=12)	MCG (n=7)	CG (n=5)	*p*
Age (years) (M, SD)	67.67 (3.70)	58.57 (4.50)	66.40 (1.95)	.343[b]
Education (years) (M, SD)	12.33 (3.87)	12.57 (2.88)	12.00 (5.34)	.755[b]
Feminine, n (%)	6 (50.00)	2 (28.60)	4 (80.00)	.149[b]
$VO_{2peak\ mL.Kg\text{-}1.min\text{-}1}$ (M, SD) at baseline	29.04 (4.65)	29.31 (1.27)	28.66 (7.53)	.639[b]
Diagnoses and medical conditions, n (%)				
Hypertension	9 (75.00)	7 (100)	2 (40.00)	.106[b]
Cholesterol	4 (33.33)	2 (25.57)	2 (40.00)	.755[b]
Bone problems	2 (16.67)	1 (14.29)	1 (20.00)	.876[b]
Prostate problems	1 (8.33)	0	1 (20.00)	.639[b]
Thyroid problems	1 (8.33)	0	1 (20.00)	.639[b]
Sleep apnea	1 (8.33)	1 (14.29)	0	.755[b]
Prescribed medication, n (%)				
Antihypertensives	9 (75.00)	7 (100)	2 (40.00)	.106[b]
Statins	5 (41.67)	3 (25.00)	2 (40.00)	1.00[b]
Psychiatric medication	1 (8.33)	0	1 (20.00)	.639[b]
$\Delta VO_{2peak\ mL.Kg\text{-}1.min\text{-}1}$ (M, SD)	-0.78 (3.211)	-1.03 (2.62)	-0.42 (4.00)	.755[a]
ΔTMT-A (M, SD)	3.33 (12.70)	4.07 (13.80)	2.30 (12.47)	.825[a]
ΔTMT-B (M, SD)	11.82 (40.82)	2.27 (43.10)	25.20 (37.57)	.362[a]
ΔSymbol search (M, SD)	6.25 (12.68)	7.00 (15.66)	5.20 (8.47)	1.00[b]
ΔDigit span forwards (M, SD)	0.25 (1.91)	-0.14 (2.04)	0.80 (1.79)	.426[a]
ΔDigit span backwards (M, SD)	0.33 (1.50)	-0.14 (1.46)	1.00 (1.41)	.432[b]
ΔVerbal paired associates II (M, SD)	-0.67 (1.50)	-1.29 (1.60)	0.20 (0.84)	.090[a]

[a]: two-independent sample Student t-test. [b]: Mann Whitney-U test.

* $p < .05$.

Table 7

Correlations Between Variations in Physical Fitness and Variations in Neurocognitive Performance

Variable	*n*	1	2	3	4	5	6	7	8	9	10	11
1. ΔVO_{2peak} $mL \cdot Kg^{-1} \cdot min^{-1}$ [a]	12	-										
2. ΔAndroid Fat Mass %[a]	18	.07	-									
3. ΔGynoid Fat Mass %[a]	18	-1.00***	.30	-								
4. ΔAndroid-gynoid Ratio[a]	18	1.00***	.46	-.65*	-							
5. ΔLean Mass %[a]	18	.95**	-.54	-.12	-.29	-						
6. ΔTMT-A[a]	18	.28	.39	.36	.16	.04	-					
7. ΔTMT-B[a]	18	-.43	-.03	-.28	.46	-.25	-.11	-				
8. ΔDigit Span Forwards[a]	18	1.00***	.01	-.50	.53	-.02	-.25	.13	-			
9. ΔDigit Span Backwards[a]	18	-.53	.17	-.24	.14	-.04	.02	-.25	-.38	-		
10. ΔVerbal Paired Associates II[a]	18	1.00***	-.16	-.34	.31	.18	-.20	.63**	.27	-.23	-	
11. ΔSymbol Search[b]	18	.37	.12	.33	-.06	-.17	-	-	-	-	-	-

Note. Pearson's partial correlations for parametric and Kendall's tau-b bivariate correlations for non-parametric variables. Partial correlations with were controlled for sex, age, education, attendance, psychiatric medication and ΔTotal body fat %. TMT-A and TMT-B decreasing time to complete is conceived as increasing performance.

[a]: Pearson's partial correlations. [b]: kendall's tau-b bivariate correlation.

* $p < .05$. ** $p < .01$. *** $p < .001$.

Discussion

Current study aims at clarifying physical fitness and cognitive effects of MCT intervention compared to an active CG, in Portuguese cognitively healthy community-dwelling elderly. Main results revealed that MCT was, compared to CG, effective in improve MVPA and decrease SED of participants. It presented no differential effect in physical fitness (anthropometry and aerobic capacity), neurocognitive functioning or emotional symptomatology, not supporting the predicted hypothesis. Moreover, CRF was associated with memory.

MCT presented no effects in anthropometry. There was a slightly decrease in fat mass % and increase in lean mass % for both groups, with greater extent in MCT, according to hypothesis. Regarding fat distribution, MCG slightly decreased android and gynoid fat percentages whilst CG slightly increased them. According to this tendency, there is preliminary evidence of MCT benefits in healthy older women in decreasing BMI and body fat percentage (Shiotsu & Yanagita, 2018). In adults, in which sex plays a role in obtained benefits (Sanal et al., 2013) and in elderly clinical samples (Chen et al., 2017; Nielsen et al., 2019; Sampaio et al., 2019; Thomas et al., 2017; Villareal et al., 2011, 2017). The lately reported decreases in body fat and body weight and increases in lean body mass, unevenly. Sex and BMI at baseline may have influenced current results. Previous evidence in overweight, reported MCT effectiveness in decreasing body fat; in obesity, in increasing lean mass and in appropriate weight, showed no anthropometry effects (Bocalini et al., 2012).

Variations between VO_{2peak} were correlated with gynoid fat %, android-gynoid ratio and lean mass %. All are physical fitness components, expected to improve with exercise (ACSM 2018). Correlations between variations in anthropometry and neurocognitive function were not found. Gynoid fat almost positively correlated with processing speed. Android-gynoid ratio almost positively correlated with short-term memory. The link between anthropometry and cognition remains controversial. Forte et al., (2017), proposed a positive link between greater adiposity and EF, particularly gynoid fat and working memory. Similarly, the tendency of our results points to a greater relevance for gynoid fat. And a more likely role of fat distribution compared to central adiposity, given that associations with android fat were not near significance. The role of anthropometry, particularly fat distribution, is still ambiguous. “The obesity paradox” in aged population refers to a relationship between excess adiposity and favorable health outcomes (Braun et al., 2015; Skinner et al., 2017), such as decreased risk for cognitive decline and better cognitive function with increased central adiposity (Bagger et al., 2004; Kerwin et al., 2010; Razay et al., 2006; Skinner et al., 2017). Contrarily, there is evidence pointing to an increased risk of cognitive decline and poorer cognitive performance with abdominal fat, overweight or obesity (Gustafson et al., 2003; Papachristou et al., 2015; Razay et al., 2006; N. West & Hann, 2009). A non-linear J-shaped relationship between adiposity and cognition may be responsible for this: normal weight and obesity are associated with poorer cognitive performance relative to overweight (Kuo et al., 2006). Similarly to CVD, body fat distribution may play a differential role in cognition. Android fat is a risk factor for CVD (Vague, 1996) while gynoid fat is protective of it, metabolic diseases and probably cognitive impairment (Dore et al., 2008; N. West & Hann, 2009; Yoon et al., 2012).

Current MCT sacrificed aerobic component to include strength and balance training, given achievement of possible differential physical and cognitive benefits. MCT was not effective at improving CRF since MCG significantly decreased VO_{2peak}. Previous MCT interventions failed to improve aerobic fitness (Komulainen et al., 2010; Nielsen et al., 2019). While other succeeded (Sampaio et al., 2019; Villareal et al., 2011), indicating that combining resistance training to aerobic training would not significantly affect improvements in CRF, while improving strength (Burich et al., 2015), constituting greater improvements in physical fitness. These discrepancies and our results may be influenced by differential methodologies to assess CRF, GXT with the Bruce Modified Protocol seems an adequate for elderly (ACSM, 2018). Also lack of adequation of aerobic training to the optimal heart rate reserve (HRR) or duration, not controlled in the current study. ACSM (2018) recommends attaining 55-85% of HRR, while a meta-analysis proposes 66%–73% HRR, in a program 3–4 times a week for 40-50 minutes per sessions, during 32-36 weeks (Huang et al., 2016).

Variations in CRF were positively associated with variations in short-term and long-term memory. Similarly, one MCT failed to improve CRF and it still predicted lower incidence of impaired memory (Komulainen et al., 2010). CRF and cognition have been associated cross-sectionally and epidemiologically (Barnes et al., 2003; Edwards & Loprinzi, 2017; Farrell et al., 2018; Freudenberger et al., 2016), indicating that CRF may be a link between PA and cognition, even if exclusively for elderly ≥70 years (Bherer et al., 2019). However, the role of CRF in cognition needs further clarification.

Both groups decreased semantic fluency and MCG decreased working memory performance, both expected to be affected by aging (Blazer et al., 2015; Cavaco et al., 2013a). Therefore, MCT was not effective in improving neither maintaining, neurocognitive functioning. Previous MCT have failed to improve neurocognitive functioning (Ansai & Rebelatto, 2015; Komulainen et al., 2010). Others reported improvements in EF, episodic memory and processing speed (Bherer et al., 2019; Nouchi et al., 2014) or, at least, the maintenance of global cognition and processing speed (Arrieta et al., 2020). Cardiorespiratory hypothesis (Dustman et al., 1984; Kramer et al., 1999) can partially explain our results since exclusively interventions effective in improving CRF, would be effective in improving cognition. Additionally, professionals felt lack of motivation in the post-training assessment.

Although there is a tendency to decrease anxiolytic and depressive symptomatology, MCT was not effective in decreasing them. The low baseline symptoms may contribute to the lack of significant effect. Other MCT have failed to improve emotional symptomatology (Ansai & Rebelatto, 2015) and majority of PE interventions with healthy or clinical samples report mixed results (El-Kader & Al-Jiffri, 2016; Laredo-Aguilera et al., 2018; Murri et al., 2018; Overdorf et al., 2016; Sobol et al., 2018; Song & Yu, 2019; Tarazona-Santabalbina et al., 2016; Zhang et al., 2014). Contrarily, PA and PE benefits in emotional symptoms have been widely revised (Carek et al., 2011; Jayakody et al., 2014; Mochcovitch et al., 2016). PA seems a protective lifestyle factor for them (Hiles et al., 2017). And PA (Cassidy et al., 2004; Overdorf et al., 2016), PE (McHugh & Lawlor, 2012) and resistance training (Gordon et al., 2018; Volaklis et al., 2019) have all been associated with better psychological well-being (reduced depression, anxiety and perceived stress).

PE interventions may be in the right direction to promote healthy and successful aging. For it, healthy samples should be preferred. We addressed the question of the "optimal program", as a multicomponent training, and the possible influence of physical fitness in cognition, increasing knowledge for researchers and stakeholders to adequate exercise prescriptions to the needs of each population. Nonetheless, much is yet to be discovered. The pursuit of the "optimal program" and confirmation of our findings must be addressed with larger samples RCTs methodologically well-designed. The mechanism(s) by which PE and PA influence the brain and cognition in elderly are still in discussion. And normative standards for CRF in treadmill in healthy elderly seem urgent in the pursuit of rigor. With the pilot study, we aimed at learning and reflecting about future clinical trials. Thereby, strengths, limitations and guidelines are reviewed in detail.

Main strength of a pilot study is allowing to withdraw conclusions with less resources. MCT is the least studied modality of PE. Including an heterogenous sample provides a more natural representation of the elderly population, improving external validity and testing the universal effect of exercise. There are several methodological strengths that can be identified: previous planning of PE by trained professionals improves chances of success and adequation of intervention; choosing an active CG allows a true comparison of the effects of different exercise modalities; objective assessments of PA, CRF and anthropometry allows cross-investigations comparisons; assessment of baseline characteristics, including PA, and monitoring PA in PE sessions.

We faced two main difficulties. First was finding eligible participants: healthy and non-medicated elderly. Second was adherence and motivation. Participants gave up the intervention or missed sessions, refused to participate or were unmotivated while doing assessments procedures.

Our findings must be interpreted carefully. Several limitations and validity treats need to be acknowledged. Sample was heterogeneous with small sample size. Some clinical diagnosis and medications, cut-off scores of GAI, GDS and MOCA were not exclusion criteria. Heterogeneity raises external validity but can constitute an internal validity treat. Diseases including obesity and medication, e.g. antihypertensives, influence cognitive function and CRF (ACSM, 2018; Brawner et al., 2004; Sobol et al., 2018; M. West et al., 2015). An objective measure of brain functioning or structure (e.g. brain image acquisition) was not included and more than one psychologist conducted the cognitive assessment. Delivery of intervention did not occur as planned for every session. Physical fitness could have been more broadly assessed by including a strength assessment, as senior fitness test (SFT) (Rikli & Jones, 1999, 2013), which has normative functional fitness standards for Portuguese elderly (Marques et al., 2014). To our knowledge, normative standards for CRF in treadmills exists for other populations (ACSM, 2018), lacking for Portuguese. It could have been important to compare how fit our participants were, compared to Portuguese. Participants were not randomly assigned to groups and majority participated in CG before MCT. Previous belonginess could influence participants motivation regarding raising frequency and modality of exercise.

Nutrition as a compensatory strategy to regulate energy expenditure exercise-induced (Blundell et al., 2015; King et al., 2008) was not monitored.

As guidelines for future research aiming at understanding PE effects in healthy elderly, we propose a trade-off between exclusion criteria according to the goal of investigation. If the goal is understanding the broad effects of exercise, a more naturalistic and heterogeneous sample should be preferred. For a clinical trial, eligible participants should be initially screened. Exclusion criteria should be highly controlled, we propose: cognitive impairment (MOCA>cut-off score); GAI or GDS above cut-off scores; BMI>25; history of neurodegenerative disorders, head injury, stroke, epilepsy, neurological or psychiatric disorder; cardiac, respiratory, motor problems or others that are contraindications for CRF evaluation; presence of a visual, auditory or language impairment or any kind of medication that could influence either cognitive function or proposed assessment. Participants should be randomly assigned and received compensation for their participation. It would be interesting to include an active and a passive CGs, with future counterbalance of exercise interventions. We recommend objective assessments to reduce error and provide a true comparison for future research. Physical fitness could be assessed by Bruce modified protocol in a treadmill for CRF and additional measures of SFT (if strength training is included) and compared to normative values. Anthropometry could use DEXA. Cognitive function should include an objective measure (brain image acquisition may serve this purpose) and a brief and straight to the point neurocognitive protocol. Current MCT let us provide a suggestion for memory. Evaluators/psychologist should be the same in all time-points. Delivery of intervention should be highly monitored. Nutrition (e.g. food diary) and PA at beginning, end and throughout the intervention should be monitored. In-session PA levels is recommended to understand the effectiveness of the exercise intervention. As recommended for ACSM (Garber et al., 2011), physical fitness at baseline should be used to create an individually-tailored intervention and monitored to adjust it, if necessary.

Combining aerobic and resistance training is a promising tool to promote successful aging. Therefore, multicomponent training and CRF’s role in cognition should be further investigated.

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Appendix 1

Universidade do Minho

SECVS

Subcomissão de Ética para as Ciências da Vida e da Saúde

Identificação do documento: SECVS 120/2016

Título do projeto: *Estudo dos efeitos da atividade física na estrutura e no funcionamento cerebral*

Investigador(a) responsável: Anabela Silva Fernandes, Investigadora, Escola de Psicologia, Universidade do Minho; Professora Doutora Adriana Sampaio, Centro de Investigação em Psicologia (CIPsi), Escola de Psicologia

Outros investigadores: Professora Doutora Maria Joana Mesquita Cruz Barbosa de Carvalho, Centro de Investigação em Actividade Física, Saúde e Lazer da Faculdade de Desporto da Universidade do Porto (FADEUP)

Subunidade orgânica: Centro de Investigação em Psicologia (CIPsi), Escola de Psicologia, Universidade do Minho

Outras Unidades: CIAFEL - Centro de Investigação em Actividade Física, Saúde e Lazer da Faculdade de Desporto da Universidade do Porto (FADEUP)

PARECER

A Subcomissão de Ética para as Ciências da Vida e da Saúde (SECVS) analisou o processo relativo ao projeto intitulado *"Estudo dos efeitos da atividade física na estrutura e no funcionamento cerebral"*.

Os documentos apresentados revelam que o projeto obedece aos requisitos exigidos para as boas práticas na experimentação com humanos, em conformidade com o Guião para submissão de processos a apreciar pela Subcomissão de Ética para as Ciências da Vida e da Saúde.

Face ao exposto, a SECVS nada tem a opor à realização do projeto.

Braga, 02 de maio de 2017.

A Presidente

MARIA CECÍLIA DE LEMOS PINTO ESTRELA LEÃO

Assinado de forma digital por MARIA CECÍLIA DE LEMOS PINTO ESTRELA LEÃO
DN: c=PT, o=Cartão de Cidadão, ou=Cidadão Português, ou=Autenticação do Cidadão, sn=DE LEMOS PINTO ESTRELA LEÃO, givenName=MARIA CECÍLIA, serialNumber=BI014512203, cn=MARIA CECÍLIA DE LEMOS PINTO ESTRELA LEÃO
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