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Dual Task Multimodal Physical Training in Alzheimer's Disease: Effect on Cognitive Functions and Muscle Strength

Treinamento Físico Multimodal com Dupla Tarefa na Doença de Alzheimer: Efeito nas Funções Cognitivas e na Força Muscular

Bruno Naves Ferreira[1]
Emmanuel Dias de Sousa Lopes[2]
Isadora Ferreira Henriques[1]
Marina de Melo Reis[3]
Amanda Morais de Pádua[1]
Karina de Figueiredo[3]
Fernanda Aparecida Lopes Magno[1]
Flávia Gomes de Melo Coelho[1,3]

Abstract – The aim of this study was to evaluate the effects of dual task multimodal physical training (MPT) on the cognitive functions and muscle strength in older adults with AD. Participants were 19 subjects with AD in the mild and moderate stages, divided into training group (TG) and control group (CG). The TG performed dual task MPT for 12 weeks. Subjects were evaluated at the pre- and post-intervention moments. The Mini Mental State Examination (MMSE), Clock Drawing Test (CDT) and Frontal Assessment Battery (FAB) were used to assess cognition. For muscle strength, the Chair Lift and Sit Test (CLST) and Manual Grasp Force (MGF) were used. The Wilcoxon test was used to analyze pre and post intragroup moments. The TG showed a significant improvement in FAB and CLST ($p \leq 0.05$) and a tendency to improve the MMSE score ($p \leq 0.08$). The CG showed significant improvement in CLST ($p \leq 0.05$). Dual task MPT improves the frontal cognitive functions and lower limb muscle strength of older adults with AD.

Key words: Alzheimer disease; Cognition; Exercise; Muscle strength.

Resumo – *Objetivou-se avaliar os efeitos do treinamento físico multimodal (TFM) com dupla tarefa nas funções cognitivas e força muscular de idosos com DA. Participaram 19 indivíduos com DA no estágio leve e moderado, divididos em grupo treinamento (GT) e grupo controle (GC). O GT realizou TFM com dupla tarefa por 12 semanas. Os idosos foram avaliados no momento pré e pós-intervenção. Para avaliação da cognição foram utilizados o Mini Exame do Estado Mental (MEEM), Teste do Desenho do Relógio (TDR) e Bateria de Avaliação Frontal (BAF). Para a força muscular o Teste de Levantar e Sentar da Cadeira (TLSC) e Força de Preensão Manual (FPM). O teste de Wilcoxon foi utilizado para analisar os momentos pré e pós-intragrupos. O GT apresentou melhora significativa na BAF e TLSC ($p \leq 0,05$) e tendência de melhora no escore do MEEM ($p \leq 0,08$). O GC apresentou melhora significativa no TLSC ($p \leq 0,05$). O TFM com dupla tarefa melhorou as funções cognitivas frontais e a força muscular de membros inferiores de idosos com DA.*

Palavras-chave: *Cognição; Doença de alzheimer; Exercício; Força muscular.*

1 Federal University of Triângulo Mineiro. Graduate Program in Physical Education. Uberaba, MG. Brazil.

2 Federal University of Triângulo Mineiro. Graduate Program in Health Care. Uberaba, MG. Brazil.

3 Federal University of Triângulo Mineiro. Department of Sport Sciences. Uberaba, MG. Brazil.

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INTRODUCTION

The aging of the Brazilian and world population is a contemporary fact, which has caused an increase in chronic degenerative diseases that affect the elderly population, among them Alzheimer's disease (AD)[1]. AD is a neurodegenerative disease that affects different areas of human functioning, such as cognitive, social, physical, behavioral, functional and metabolic[2], being the most common form of dementias, accounting for 60% to 80% of cases[3].

AD has two classic neuropathological biomarkers, both of which lead to neuronal death. Extracellularly, there is an excessive accumulation of beta-amyloid plaques (Aβ) that prevent the passage of cellular nutrient substrates by altering the local pH. There is formation of neurofibrillary tangles caused by hyperphosphorylation of the Tau protein in the intracellular medium, which disintegrates the microtubules of the cytoskeleton[4]. This neuronal loss in older adults with AD is the main factor that triggers memory deficit and the decline in cognitive functions[5]. In addition, older adults with AD have lower peripheral concentrations of some biomarkers such as Brain Derived Neurotrophic Factor (BDNF)[6] and Insulin Growth Factor-1 (IGF-1)[7], and higher peripheral concentrations of inflammatory biomarkers such as Interleukin-6 (IL-6) and Tumor Necrosis Factor (TNF-α) [8], which are linked to cognitive decline.

In addition to sarcopenia due to the aging process, older adults with AD present a marked decrease in the level of physical activity[9], which contributes to reduce muscle strength. Garuffi [10] points out that older adults with AD have lower strength of lower and upper limbs when compared to those without dementia.

The benefits of physical exercise in mental health have been the focus of studies in recent years, especially among older adults with cognitive impairment and AD[11-14]. Among the types of physical exercises, multimodal exercises stand out, which when associated with dual task has been shown to improve functional capacity and cognition[12]. However, there are still few studies in scientific literature that show improvement in cognition and muscle strength as a result of multimodal training in older adults with AD.

Therefore, the aim of this study was to evaluate the effects of dual-task multimodal physical training (MPT) on the cognitive functions and muscle strength of older adults with AD.

METHODOLOGICAL PROCEDURES

Study Characterization and Ethical Aspects

This is a quasi-experimental study with a quantitative approach approved by the Ethics Research Committee of the Federal University of Triângulo Mineiro (UFTM) under protocol number 1.040.482.

Sample

Margin of error of 5%, statistical power of 80% and effect size of moderate magnitude were used to calculate the sample size needed to produce representative data, resulting in minimum size of 34 participants. Thus, a wide dissemination of the "MoviMente" Extension Project (Exercise Program for Older Adults with Alzheimer's Disease) of the UFTM was carried out in a period of two years to recruit the largest number of older adults with AD. Publicity was made through media such as: television, radio, electronic media, and visits were also made to older citizens in the city of Uberaba, the Brazilian Alzheimer Association (ABRAZ, Uberaba-MG) and medical offices (neurologists, geriatricians and psychiatrists). Of the 46 older adults recruited and evaluated, only 25 met the criteria to participate in the study. During the experimental period, 06 gave up participating, and in this way, 19 participants completed the study, as shown in figure 1.

Inclusion criteria were: elderly with clinical diagnosis of AD through medical certificate, level of severity of mild or moderate dementia according to the Clinical Dementia Rating Score (CDR), availability for participation of evaluations, and participants and caregivers who agreed to the study procedures signed the Free and Informed Consent Form.

Exclusion criteria were: presence of coronary disease, cardiac arrhythmias, uncontrolled hypertension, angina symptoms, absolute restriction to physical exercise, visual and auditory impairment, dizzying syndrome or other limitations that made locomotion difficult, concomitant neuropsychiatric conditions, non attendance in the pre-scheduled evaluations and attendance of less than 70%.

After inclusion, participants were divided for convenience into control group (CG) and training group (GT), which included 8 female participants and 3 male participants, totaling 11 participants and the CG included 7 female participants and 1 male female participant, totaling 8 female participants. The CG was instructed to follow their normal routine without the practice of scheduled physical exercises, and GT participated in the dual task MPT.

Evaluation Protocol

At the first moment, anamnesis with participants and their respective caregiver or relative was performed to identify socio-demographic data: age, gender, schooling, marital status, profession, country of birth, children, religion, address and telephone numbers; and clinical data: time of illness, practice of physical activity, responsible physician, caregiver, use of glasses and / or hearing aid, surgeries performed, comorbidities, restriction of physical exercise and medications in use.

After inclusion of participants, two evaluations were scheduled, one at the pre-intervention and the other at the post-intervention moment, with a twelve-week interval between them.

Three instruments were used to assess cognition:

a) Mini Mental State Examination (MMSE): an instrument composed of questions grouped into seven categories, each one planned with the

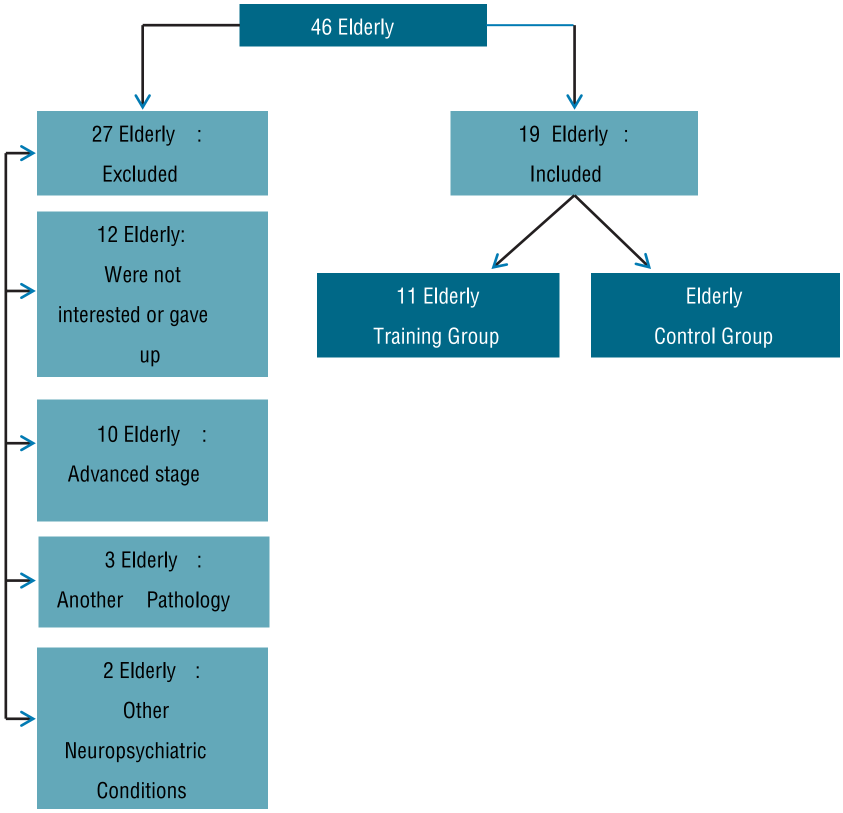

Figure 1. Illustrative scheme for sample recruitment.

purpose of evaluating specific cognitive functions, namely: temporal orientation, spatial orientation, three word register, attention and calculation, recall of the three words, language and visuoconstructive ability. The MMSE score varies from 0 to 30 points according to the years of schooling, with lower values indicating possible cognitive deficit[15].

b) Clock Drawing Test (CDT): task of drawing a clock with the insertion of pointers marking a certain time (2h45m), and is intended to measure executive functions (planning, abstract thinking, logical sequence and executive processing monitoring). The test is based on a score from 0 to 10 points, and higher scores mean better performance in the executive functions evaluated[16].

c) Frontal Assessment Battery (FAB): evaluates frontal cognitive functions composed of 6 subtests: "Similarities" (abstract reasoning), "Lexical Fluency" (mental flexibility), "Motor Series" (programming), "Conflicting Instructions" (sensitivity to interference), "Go - will not" (inhibitory control) and "Grasp behavior" (primitive reflex). It ranges from 0 to 18 points, and high scores mean better performance in frontal functions[17].

Two tests were used to evaluate muscle strength:

a) Chair Lift and Sit Test in 30 seconds (CLST): the test begins with the participant sitting in the middle of the chair, with the back straight and feet flat on the floor. The arms are crossed against the thorax. At the sign "Attention! Go!", the participant stands up, standing upright and then returning to a fully seated position. The subject is encouraged to sit completely the highest number of times in 30 seconds[18].

b) Manual Grasping Strength (MGS): evaluated through an adjustable and calibrated dynamometer with scale from 0 to 100 kilograms. The subject is placed in the orthostatic position, and the appliance was comfortably fixed in the forearm line, being parallel to the longitudinal axis of the body. The proximal interphalangeal joint of the hand should be adjusted under the bar that is then tightened between the fingers and the tenar region. During manual grasping, the arm remains immobile, with only the flexion of the interphalangeal and metacarpophalangeal joints. Three measures were performed in the dominant hand and mean values were obtained[19].

Dual Task Multimodal Physical Training Protocol

The dual-task MPT protocol was performed three times a week on non-consecutive days for 12 weeks. Each session lasted one hour. Sessions were divided into activities and each day of the week was focused on different components of functional capacity, namely: a) aerobic capacity and muscular strength; b) aerobic capacity, agility and balance, and c) muscle strength, agility and balance.

There was a progression during the protocol, increasing the difficulty of exercises, intensity and volume, gradually and according to the capacity of each participant.

The aerobic training intensity was maintained between 65% and 75% of the maximum heart rate predicted for age, characterizing in general training with aerobic predominance of moderate intensity. Heart rate was assessed during sessions through the use of a Polar frequency meter.

In activities of balance and agility, progression occurred due to the degree of difficulty of exercises, requiring an increase in the motor capacity of participants. In addition, from the seventh week, cognitive tasks were included simultaneously with motor tasks, that is, dual task. Participants were instructed to perform a motor task (bounce a ball, walk, weight exercises) and at the same time perform cognitive tasks, such as saying words according to semantic criteria (names of animals, fruits, people and objects), counting and naming figures. There was also progression in cognitive tasks, for example, increase in the number of figures to be named and inclusion of countdown.

In weight training, progression occurred every two weeks, and week 1 and 2 were adaptive (2 sets and 8 to 10 repetitions), in weeks 3 and 4, there was an increase in the number of repetitions (2 sets and 10 to 15 repetitions), in weeks 5 and 6, there was an increase of sets (3 sets and 10 to 15 repetitions), in weeks 7 and 8, there was an increase of load (3 sets and 10 to 15 repetitions and increase of the weight of dumbbells and ankle weights), in weeks 9 and 10, there was inclusion of exercises with greater degree of difficulty, and in weeks 11 and 12, increase in exercise loads, as presented in Box 1. Two upper limb exercises (MMSS) and two lower limbs exercises (MMII) were used for each session. The load increase was according to the individuality of each participant, being guided by the participant's subjective perception of effort and by the perception of the responsible physical education professional.

Box 1. Progression of training with weights

Week	1	2	3	4	5	6
Load	2x 8 to 10 rep		2x 10 to 15 rep		3x 10 to 15 rep	
Week	7	8	9	10	11	12
Load	3x 10 to 15 rep + Increase load		3x 10 to 15 rep + New exercises		3x 10 to 15 rep Increase load	

Statistical analysis

Descriptive data analysis was performed by mean and standard deviation. For the sample characterization variables, the U Mann Whitney test was used to verify differences between groups (TG and CG) at the time of intervention, Mann Whitney U test for intergroup and Wilcoxon test for intragroup comparisons.

RESULTS

The study had the participation of 19 older adults, 4 men and 15 women in two groups, 11 in the TG and 8 in the CG. The U Mann Whitney test pointed out that both groups were similar at pre-intervention time for all variables. Table 1 presents the sociodemographic and clinical characteristics.

Table 1. Median and upper and lower limits of sociodemographic and clinical characteristics of training (TG) and control (CG) groups

Variables	TG (n=11)	CG (n=8)	p
Age (years)	78 (62-85)	76,5 (63-89)	1.0
Schooling (years)	5 (1-16)	4,5 (4-16)	1.0
Time of disease (months)	24 (6-48)	30 (8-120)	0.31
CDR (scores)	1 (1-2)	1 (1-2)	0.77

TG: Training group; GC: Control group; CDR: Clinical Dementia Rating Score.
p: U-Mann Whitney test

Regarding cognitive variables, TG showed significant improvement in FAB ($p \leq 0.05$) and tendency to improve the MMSE score ($p \leq 0.08$), with no significant difference in CDT ($p = 0.931$). The CG did not present significant results in any of the cognitive variables (Table 2).

Regarding the strength variables, the TG showed a significant improvement in CLST ($p = 0.006$). CG presented similar results to TG in the strength variables, evidencing improvement in CLST ($p = 0.033$) and non-significant results in MGF (Table 3).

Table 2. Median and upper and lower limit of cognitive variables analyzed in the pre- and post-intervention moments between training (TG) and control (CG) groups.

Variables	TG (n=11)		CG (n=8)	
	Pre	Post	Pre	Post
MMSE (scores)	17 (13-27)	21 (12-26)**	16 (5-29)	17,5 (13-30)
CDT (scores)	3 (1-10)	5 (2-10)	4 (1-10)	3 (2-10)
FAB (scores)	9 (6-14)	12 (4-16) *	9,5 (3-18)	10,5 (9-18)

*: Wilcoxon p≤0.05; **: Wilcoxon p≤0.08; MMSE: Mini Mental State Examination; CDT: Clock Drawing Test; BAF: Frontal Evaluation Battery.

Table 3. Median and upper and lower limit of muscle strength variables analyzed in the pre- and post-intervention moments between training (TG) and control (CG) groups.

Variables	TG (n=11)		CG (n=8)	
	Pre	Post	Pre	Post
CLST (scores)	10 (5-13)	12 (7-19)*	10 (0-14)	13 (0-16)*
MGF (kg)	22 (11-40)	23 (13-42)	23 (14-41)	23 (18-42)

*: Wilcoxon p≤0.05; CLST: Chair Lift and Sit Test; MGF: Manual Grasp Force.

DISCUSSION

Our main finding was that dual task MPT was able to improve the executive functions in the TG. These improvements bring significant benefits in attention, planning, organization, strategy creation, operational memory and thought flexibility. The CG did not present significant response to cognitive variables.

Corroborating the results found, Coelho et al. [20] performed dual task MPT for 16 weeks with frequency of 3 times a week on nonconsecutive days and found improvement in the executive functions in the TG, specifically in abstraction, organization, motor sequence and performance in attention. The CG had significant decline in planning, organization, and motor sequencing. Another study with similar methodology[11] also found positive results in the frontal cognitive functions in the TG.

In addition, these two studies found significant CDT values in the TG, which was not observed in the present study. Possibly, the duration of the proposed training protocol of 12 weeks was not sufficient to promote significant CDT results. It is noteworthy that in the studies above, double task was performed for a period of 16 weeks and for 6 weeks in the present study.

The MMSE is an instrument frequently used to evaluate cognitive functions in elderly patients with AD[12]. Our results did not show improvement in MMSE in none of the groups; however, a trend in the TG (p≤0.08) was observed. However, Vreugdenhil et al.[21] carried out a study with 40 elderly patients with AD, allocating 20 participants in the TG and 20 in the CG. The TG performed a 16-week MPT and showed significant improvement in cognitive functions through MMSE, while the CG presented a significant decline. Corroborating these results, the literature presents similar studies[13,22]. Nascimento et al.[23] carried out a study with MPT for 24 weeks and observed that the TG showed reduction in the neuropsychiatric symptoms of AD, increasing the global cognitive functions and improving the ability to perform daily activities.

The scientific literature has pointed out that multimodal physical training seems to be the most appropriate type of exercise to promote improvements in the cognitive functions of older adults with AD, corroborating our study, which pointed out progress in the cognitive functions of patients with AD after dual task MPT. In this sense, Coelho[24] indicates possible mechanisms by which intervention provided benefits in frontal functions, among them: a) frontal cognitive functions were stimulated during intervention - the "physical exercise demonstration" requires attention and abstraction, "continuous execution" requires motor sequencing, and "permanence in the task" requires self-control; b) the dual task also provided activation of cognitive functions and c) cognitive stimulation associated with neurobiological, psychological and social effects of physical exercise may have contributed to the improvement of cognitive functions.

The improvement in the performance of frontal cognitive functions of patients with AD is extremely important, since they present a deficit of executive functions, characterized by the decrease in the capacity of solving problems, judgment of what is right or wrong, mental flexibility, organization and self-control, presenting a decline with the disease progression. These losses make these individuals dependent to perform instrumental activities that require cognition, such as cooking, shopping, handling money, driving, among others, leading to loss of autonomy[25]. With the positive effects of exercise on frontal cognitive functions, patients with AD consequently increase their capacity to perform instrumental tasks, which provides benefits in autonomy and directly interfere in aspects of their social life.

Regarding muscle strength, our study showed an increase in lower limb strength in the TG, but did not present a significant result in upper limb strength. However, the CG also showed positive results in lower limb strength. The CG was instructed to follow their normal routine, without performing any physical exercise program; however, the amount of physical activity of the control group was not controlled, which may be considered a study limitation. There are only few studies evaluating the effect of MPT on the strength of older adults with AD. Nascimento[26] applied a 16-week MPT with a sample composed of 17 participants in the TG and 18 in the CG with no satisfactory results in upper and lower limb strength for both groups. In contrast, the study by Coelho[24] showed improvements in the lower limb strength of elderly patients with AD after 16 weeks of dual task MPT.

Both elderly without dementia and those in the pre-dementia and early stages of AD have compromised motor function[27], with a decline in muscle strength. Thus, the positive result observed in our study about lower limb strength is important for maintaining and increasing muscular strength for this population, since it will aid in the vital activities of their everyday life such as: sitting and standing, walking with autonomy and safety, among other everyday activities[28]. Regular physical exercise is considered a beneficial alternative to attenuate the loss of muscular strength with aging, bringing autonomy and social insertion[29], in addition to reducing the risk of falls in older adults with AD[30].

Although our study has demonstrated the positive effects of dual-task multimodal physical training in AD patients, it is necessary to consider that this study has limitations, among them the small number of participants and the lack of sample randomization. These procedures were unavoidable due to the difficulty of recruiting older adults with AD and the difficulty of keeping participants in the program. It is noteworthy that caregivers and family members were not always available to take participants to the program or to carry out evaluations.

CONCLUSION

Dual task multimodal physical training provided improvements in frontal cognitive functions and muscle strength in the lower limbs of elderly individuals with AD. It is important to emphasize that non-pharmacological interventions, such as physical exercise, have provided a beneficial impact in attenuating cognitive decline and improving motor function in elderly individuals with AD, representing a valuable contribution to this population.

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CORRESPONDING AUTHOR

Bruno Naves Ferreira
Programa de Pós-Graduação em Educação Física
Universidade Federal do Triângulo Mineiro
Av. Tutunas 490, Uberaba, Brasil
CEP 38061-500.
E-mail: ferreirabnef@gmail.com