

Is Strength Training as Effective as Aerobic Training for Depression in Older Adults? A Randomized Controlled Trial

Helena S. Moraes^{a, b} Heitor S. Silveira^a Natacha A. Oliveira^a
Eduardo Matta Mello Portugal^a Narahyana B. Araújo^b Paulo E. Vasques^a
Astrid Bergland^c Tony M. Santos^d Knut Engedal^e Evandro S. Coutinho^f
Felipe B. Schuch^g Jerson Laks^{b, h} Andrea C. Deslandes^{a, b}

^aLaboratório de Neurociência do Exercício, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil; ^bPrograma de Pós-Graduação em Psiquiatria e Saúde Mental, Instituto de Psiquiatria, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil; ^cDepartment of Physiotherapy, Faculty of Health Sciences, Oslo and Akershus University College of Applied Sciences, Oslo, Norway; ^dDepartamento de Educação Física, Universidade Federal de Pernambuco (UFPE), Recife, Brazil; ^eNorwegian Centre for Aging and Health, Vestfold Health Trust and the University of Oslo, Oslo, Norway; ^fInstituto de Medicina Social da Universidade do Estado do Rio de Janeiro (UERJ), Rio de Janeiro, Brazil; ^gDepartamento de Métodos e Técnicas Desportivas, Universidade Federal de Santa Maria, Santa Maria, Brazil; ^hPrograma de Pós-Graduação em Biomedicina Translacional, Universidade do Grande Rio (Unigranrio), Duque de Caxias, Brazil

Keywords

Mental health · Physical exercise · Elderly patients

Abstract

Background: This study aimed to compare the effects of aerobic training (AT), strength training (ST) and low-intensity exercise in a control group (CG) as adjunct treatments to pharmacotherapy for major depressive disorder (MDD) in older persons. **Methods:** Older persons clinically diagnosed with MDD ($n = 27$) and treated with antidepressants were blindly randomized into three groups: AT, ST and a CG. All patients were evaluated prior to and 12 weeks after the intervention. **Results:** Compared with the CG, the AT and ST groups showed significant reductions in depressive symptoms (treatment response = 50% decrease in the pre- to post-intervention assessment) through the Hamilton Depression

Rating Scale (AT group: $\chi^2, p = 0.044$) and Beck Depression Inventory (ST group: $\chi^2, p = 0.044$). **Conclusion:** Adding AT or ST with moderate intensity to the usual treatment promoted a greater reduction of MDD symptoms.

© 2019 S. Karger AG, Basel

Introduction

Major depressive disorder (MDD) is a highly prevalent disorder in both high- and low-income countries. A wide variety of antidepressant medications are used to treat MDD; however, about 47% of patients respond to the first pharmacological treatment [1], and the rates of relapse and symptom recurrence are as high as approximately 80% [2]. Long-term treatment failures are also common (40–60%) [3], and 20% of patients remain with depressive

symptoms for more than 20 years [4]. Lastly, although necessary, treatment involving medication may be problematic for older persons due to the increased risk of falls, cardiovascular events, fractures, epilepsy, hyponatremia, all-cause mortality, side effects or medication interactions [5, 6].

Currently, many additional therapies are under investigation aiming at increasing the efficacy of antidepressant treatments. Since the first publications on the effects of exercise in depressed patients [7, 8], several hypotheses regarding the physiological (increased neurotransmitter synthesis, release of neurotrophic factors, changes on inflammatory and oxidant profiles) [9] and psychological (increased social contact and improved quality of life, self-esteem and functional capacity) [10] mechanisms have been developed and investigated. Systematic reviews and a meta-analysis have shown that exercise is effective in reducing depressive symptoms in subjects with high symptom loads of depression regardless of whether they have a clinical diagnosis of MDD or not [11–14].

It is known that aerobic training (AT) promotes neurophysiological effects whose results may be similar to those observed after antidepressant drug treatments [15]. On the other hand, strength training (ST) promotes improvement in functional capabilities preventing dependency in activities of daily living and improves cognitive functioning, which can also be beneficial to MDD patients [16]. A recent meta-analysis published by our laboratory demonstrated that the effectiveness of physical exercise (AT and ST) in the treatment of depression is higher in patients older than 60 years and in subjects with mild symptoms [17]. A previous randomized controlled trial has also observed a positive correlation between change in depressive symptoms and gain in muscle strength [18]. However, most studies have included only AT as an intervention. For example, among the 18 arms of the clinical trials reviewed, only 4 arms included ST. In addition, one of the arms has used low-intensity ST training (20% of 1 repetition maximum) [18]. Altogether, these issues may have contributed to the decreased effectiveness of ST. Some meta-analysis studies have shown that the antidepressant effects of exercise are not significant when only high-quality trials are analyzed [19, 20]. Previous studies have compared the antidepressant effect of the AT and ST in adults with depression, but the results were inconsistent [21–23]. Also, no study was performed in older adults. In this context, there is little evidence for the effect of ST on the depressive symptoms in older adults. Moreover, it is important to explore alternative forms of exercise since individuals with several mental illnesses

show a sedentary behavior. ST can also contribute to improving physical health and appearance as well as reduce weight, which are considered motivating factors to this population to engage physical exercise [24].

The present study aimed to compare the effects of AT, ST and low-intensity exercise (social contact/control group, CG) as adjunct treatments to pharmacotherapy in reducing depressive symptoms in older persons with MDD.

Material and Methods

Experimental Approach to the Problem

This randomized clinical trial has a duration of 12 intervention weeks. Patients ($n = 27$) were randomly assigned into three groups by a blinded investigator: AT ($n = 9$), ST ($n = 9$) and CG ($n = 7$), paired by age and baseline scores on the Hamilton scale. Two subjects were excluded from the CG, one due to a broken arm and another who underwent surgery. The incidents were not related to the research. The fracture was due to a fall in a domestic environment, and the surgery was for the treatment of breast cancer.

All patients in the two intervention groups performed 30 min of moderate-intensity physical exercise in each session as an adjunct to their current pharmacological treatment. The CG also performed 30 min in each session of low-intensity physical exercise. Adherence to treatment was controlled by the frequency in the session intervention, with participants having to attend no less than 75% of the 24 sessions in 12 weeks. The patients did not perform physical exercise outside of the treatment setting. All patients (AT, ST and CG) were assessed at pre- and postintervention time points (Fig. 1).

Subjects

The outpatients were selected from the Center for Alzheimer's Disease and Related Disorders from the Institute of Psychiatry at the Federal University of Rio de Janeiro. One hundred and fifty patients with a diagnosis of MDD were identified while undergoing treatment at our outpatient clinic. Of these, 49 subjects agreed to participate, 27 of whom were eligible to be included in the study (see Fig. 1 for a definition of eligibility). All patients were evaluated by psychiatrists and diagnosed with MDD according to the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV), excluding all possible clinical and psychiatric comorbidities. In case of doubt, a second psychiatrist reassessed the patient in order to confirm the diagnosis.

The sample size calculation was conducted considering an effect size of 0.4 [25] for both scales (Hamilton Depression Rating Scale, HAM-D, and Beck Depression Inventory, BDI). The probabilistic error considered for the three groups was $\alpha = 0.05$ (pre-specified significance level) and power = 0.80 ($1 - \beta$). The software G*Power[®] Version 3.1.9.2 was used to calculate the sample. The total sample size indicated was 64 subjects. The inclusion criteria included older persons over 60 years of age who were sedentary for more than 3 months, and those with a clinical diagnosis of MDD according to the DSM-IV. According to the American College of Sports Medicine, a sedentary lifestyle is defined as a low physical activity per week, of less than 150 min. All participants were un-

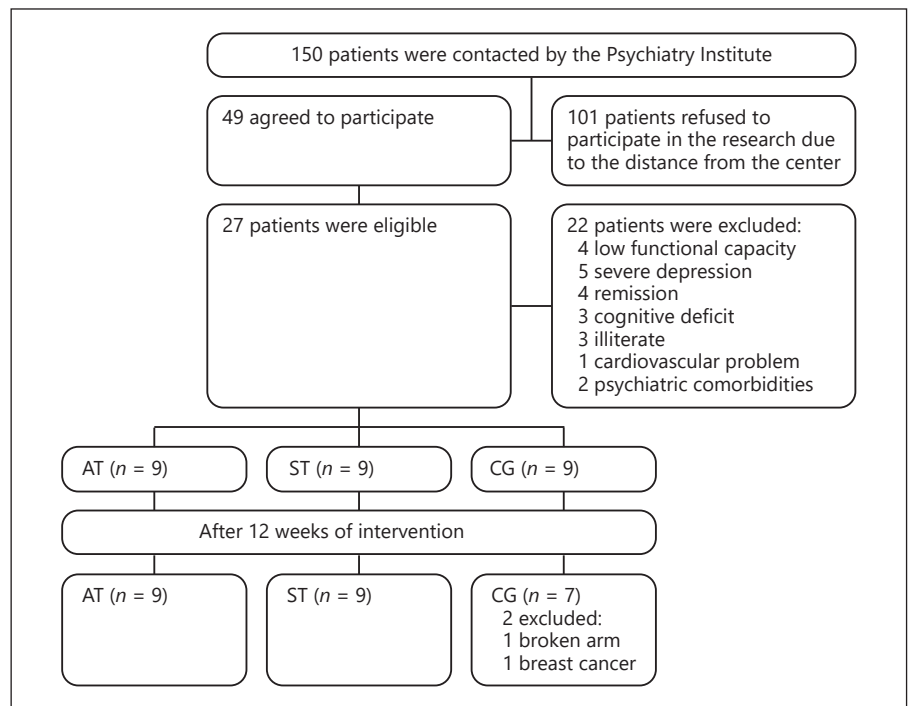


Fig. 1. Recruitment sample. AT, aerobic training; ST, strength training; CG, control group (low-intensity exercise/social contact).

dergoing clinical treatment and had been regularly using antidepressants (fluoxetine or sertraline) and anxiolytics (diazepam or clonazepam) for at least 4 weeks prior to the study, at doses within the therapeutic range. The exclusion criteria were as follows: a score higher than 18 points on the HAM-D [26]; a score less than 24 points on the Mini-Mental State Examination (MMSE) [27]; psychiatric comorbidities; cerebrovascular infarction; neurodegenerative disease; severe cardiovascular disease; illiteracy; poor mobility; balance disorders; and severe deficits in visual and/or auditory function.

As patients recruited by psychiatrists were all preserved cognitively (MMSE ≥ 24), all patients were informed and signed the consent form, without the need for authorization from a legal guardian. The authors confirm that all ongoing and related trials for this intervention are registered.

Procedures

The evaluation period lasted 1 h/day for 2 days. During the first day, the depressive symptoms were assessed. On the second day, the cardiological examination was performed, which included an electrocardiogram and maximal oxygen uptake ($VO_{2\max}$) assessment. In addition, subjects who were randomized to the ST group had another day of evaluation to determine the training intensity through the 1-repetition maximum (1RM) test.

Depressive Symptoms

The intensity of the depressive symptoms was assessed using the validated Portuguese translations of the BDI [28]. Although these assessments serve the same purpose, the two scales were selected for their specific differences. The HAM-D scale covers most aspects of psychosomatic disorders, whereas the BDI covers more emotional aspects. Moreover, the BDI is a self-assessment scale,

which enabled us to compare the self-appraisal of the depressive status with the clinician's view elicited by the HAM-D, if necessary.

The HAM-D scale has 17 items that can be scored from 0 to 4 according to the severity of the reported symptoms. Scores greater than 25 indicate severe depression; scores between 18 and 24 define moderate depression, and scores between 8 and 17 indicate mild depression.

The BDI has 21 items that can be scored from 0 to 3 according to the severity of the symptoms assessed. Scores greater than 35 indicate severe depression; scores between 20 and 34 indicate moderate depression, and scores between 11 and 19 indicate mild depression.

The remission of depressive symptoms was defined as a final HAM-D score ≤ 7 and a final BDI score ≤ 10 . A response to treatment was defined as a 50% reduction in the scale scores between the pre- and postintervention assessments. Treatment efficacy was evaluated by effect size through estimates of the outcome; treatment efficacy was defined as low (0.2–0.5), average (0.6–0.8) and high (>0.8).

Cardiovascular Test

All patients underwent resting electrocardiograms using a 3-channel electrocardiograph EP-3 Digital. Electrocardiographic tracing and the calculation of values that $VO_{2\max}$ provided were recorded and analyzed using the digital program TEB (Technology Electronica Brasileira[®]) and treadmill TEB 200/APEX 1.000 through the Ramp protocol, respectively. The protocol procedures required 3 min of warm-up with an initial speed of 2.5 km/h and 0% incline, followed by 3 min of gradual and light increments of speed and/or incline until 60% of $VO_{2\max}$ or 70% of maximum heart rate (HR_{\max}). The criteria of the American Heart Association were used to determine when to stop the test.

One-Repetition Maximum Tests

The 1RM test was applied only in the ST group. For each trial and error test, the subject performed one coordinated and complete repetition with maximum loads on the leg extension, leg curl, chest press and low row machines. If the subject performed more than 1 repetition on the estimated load, then the test was repeated with an increased load. The interval between each trial was approximately 5 min. The test was conducted by experienced sports medicine specialists. Heart rate, blood pressure and perceived exertion were monitored during the test.

Intervention

The AT group performed aerobic exercise on stationary bikes or treadmills. The intervention protocol comprised 5 min of warm-up exercise, followed by 20 min of exercise with a continuous intensity of 60% of the $VO_{2\max}$ (as predicted by the initial cardiovascular test) or 70% of the HR_{\max} calculated using the formula $HR_{\max} = 208 - (0.7 \times \text{age})$, and a 5-min deceleration period.

The ST group performed exercises for the major muscle groups, namely, the chest (chest press), back (low row), quadriceps (leg extension) and ischium (leg curl), using the machine Techno Gym® (Italy) line Selection 2009. The intervention protocol was designed to perform three sets of 8–12 repetitions on each machine with 70% of the maximum strength capacity (expected during test 1RM). As a warm-up, the first series was completed on each machine with a load less than 50% of the capacity used during training. The load progression was implemented when the patient performed the maximum number of repetitions, i.e., three consecutive times.

The CG engaged in low-intensity exercise for the same length of time (30 min/session) as the other groups (AT and ST). The CG performed 5 min of low-intensity aerobic exercises (e.g., walking on a treadmill with a predetermined speed (2.5 km/h) without inclination or cycling for 5 min without a load on a stationary bike at less than 40 cycles/min). In addition, the CG performed a series of 8 repetitions of a predetermined minimum load (one plate) on the four machines. Finally, the CG performed a series of stretches that included the lower limbs, the upper limbs, and trunk for 10 s. In this group, the exercise intensity was controlled to enable the assessment of the influence of social contact in training.

The scale of perception of effort from 6 to 20 [29] was used to quantify the subject's effort during activity. Additionally, the arterial pressure (equipment Tycos WelchAllyn® USA) and heart rate (monitor FT1 Polar® Finland) were used for measurements before, during (every 5 min) and after each training session.

The patients trained twice a week for 12 weeks and could not exceed a limit of two absences per month. The exercise routine was supervised by trained exercise physiologists and physical therapists.

Statistical Analyses

The means and standard deviation were used for the descriptive analyses. χ^2 tests were used with categorical variables (gender, medication, comorbidities, remission and response). Evaluation tests of Gaussian (Shapiro-Wilk test) and homoscedasticity (Levene's test) were used in all variables to define the statistical model. One-way ANOVAs were used to compare between groups (AT, ST and CG) at baseline for each variable: age, weight, height, educational level, MMSE, HAM-D, and BDI.

To evaluate the differences between groups (AT, ST and CG) at specific time points (pre- and postintervention), a two-way ANOVA (group and time) was used with the variables HAM-D and BDI. Remission was calculated through percent reduction of MDD symptoms below the cutoff, while response was at least 50% reduction of initial scores. The Bonferroni post hoc test was performed to identify any differences between groups. To evaluate the occurrence of remission and response, frequency analysis χ^2 was performed for all groups. The effect size was calculated for all groups to assess the magnitude of the effect of interventions on HAM-D and BDI scores. The number needed to treat (NNT) was calculated for the AT and ST groups in order to assess the clinical relative efficacy of the interventions on the HAM-D and BDI scores for response and remission [30].

The intensity and progression of training were analyzed using the index values VO_2 training (VO_{2t}) for the AT group and the total training load (TTL) for the ST group. The VO_{2t} was calculated using the formula $VO_{2t} = 0.1 \times (\text{speed} \times 16.66) + (1.8 \times (\text{speed} \times 16.66) \times \text{incline}\%) + 3.5$ with the values of speed and incline of the treadmill. The TTL is the sum of the load (plate) of all ST equipment, which includes two for the upper and two for the lower limbs. The paired test was used to evaluate the possible difference between the measurements of intensity ($VO_{2\max}$ and TTL) applied in training before and after intervention in the AT and ST groups. SPSS® 19.0 for Windows was used for all analyses, and the significance level used for this study was $p < 0.05$.

Results

Baseline Assessment

There were nonsignificant differences observed between the groups (see Table 1 for group characteristics) at baseline for age, weight, height, educational level, MMSE score, HAM-D score or BDI score. After correction of the significance level (by dividing the level by 2), results would still remain significant for comparisons of ST versus CG and AT versus CG.

Assessment of Symptoms

The evaluation of symptom remission using the HAM-D ($F = 5.71$; $p = 0.058$) and the BDI ($F = 2.77$; $p = 0.249$) scales indicated a nonsignificant difference between ST and AT groups. Symptom remission was higher in the AT and ST groups when compared to the CG (Table 2). The CG exhibited no remission according to either scale (HAM-D or BDI). Treatment response was higher in the AT and ST groups, whereas the CG showed no response following the intervention. Significant differences were observed between the AT and ST groups in comparison to the CG, by the HAM-D scale assessment ($F = 6.26$; $p = 0.044$) and BDI ($F = 6.26$; $p = 0.044$) (Table 2). A measurement of the effect size indicated that ST and AT groups presented a large effect assessed by the HAM-D ($D = 1.5$;

Table 1. Baseline characteristics of the sample

	AT (<i>n</i> = 9)			ST (<i>n</i> = 9)			CG (<i>n</i> = 7)			<i>F</i>	<i>p</i>
	range	mean	SD	range	mean	SD	range	mean	SD		
Age, years	60–78	70.88	5.94	60–81	72.89	7.06	61–77	69.28	5.28		0.582
Weight, kg	52–93	68.50	12.47	56–85	69.42	9.89	56–76	68.05	6.27	1.89	0.175
Height, cm	145–176	155.7	9.62	147–171	157.4	6.98	143–170	158.0	7.97	0.17	0.844
MMSE (score 0–30)	24–29	26.66	1.73	24–30	26.88	2.42	27–30	28.71	1.25	1.48	0.247
Gender, <i>n</i> female		8			8			5		1.14 ^a	0.565
Educational level, years	4–11	6.88	2.75	5–14	9.55	4.30	4–14	9.42	4.99		0.200
Duration of disease, years	3–9	5.55	2.24	1–7	3.77	1.64	1–7	4.00	2.16		0.326
Medication, <i>n</i>										1.15 ^a	0.825
Anxiolytics		0			0			0			
Antidepressants		8			7			4			
Both		1			2			3			
Comorbidities, <i>n</i>										11.5 ^a	0.171
Hypertension		5			6			4			
Diabetes		2			3			2			
Osteoporosis		3			3			2			

SD, standard deviation; MMSE, Mini Mental State Examination; AT, aerobic training; ST, strength training; CG, control group (low-intensity exercise/social contact). *p* < 0.05, significant difference (one-way ANOVA). The variables gender, medication and comorbidities are displayed in frequency. ^a χ^2 value.

2.8, respectively) and BDI scales (*D* = 1.7; 1.2, respectively) (Table 2). The measurement of the NNT indicated that ST and AT interventions have clinically meaningful effects, as assessed both by the HAM-D and BDI (NNT > 1.0) (Table 2).

The evaluation of depressive symptoms using the HAM-D scale demonstrated a significant interaction time \times group (*F* = 4.727; *p* = 0.014). A post hoc analysis showed significant reduction in the AT group compared to the CG (*p* = 0.005) and in the ST group compared to the CG (*p* = 0.007). A nonsignificant difference was found between the AT and ST groups (*p* = 0.991). In addition, main effects for time (*F* = 32.866; *p* = 0.001) and for group (*F* = 6.772; *p* = 0.003) were observed (Table 2).

Due to the high variability of the BDI scores, the natural log was calculated before applying the parametric model (two-way ANOVA). The assessment of symptoms using the BDI scale showed a main effect for time (*F* = 19.775; *p* = 0.001); it means that all groups exhibited reduced symptoms following the intervention. However, nonsignificant differences were found among groups (*p* = 0.104).

Training Parameters

The index used to assess the intensity and progression of AT and ST demonstrated significant differences between times (VO_{2t}, *p* = 0.001; TTL, *p* = 0.001; Fig. 2). The CG did not change the intensity parameters of the train-

ing during the intervention period. The maximum number of sessions attended was 24 for 12 weeks, and the minimum was 18 (75% of the sessions).

Discussion

This study aimed to compare the effects of AT, ST and low-intensity exercise (social contact/control group) as adjunct treatments to pharmacotherapy in reducing depressive symptoms in older persons. Following the 3-month intervention, similar improvements were observed in the groups that performed AT and ST with moderate intensity, whereas no response was observed in the CG, which performed the low-intensity exercise.

Although there is a robust evidence for the effect of exercise in depression, studies have shown different types and methodological aspects regarding exercise. Belvederi Murri et al. [32] demonstrated that combining 24 weeks of aerobic exercise including nonprogressive intensity or progressive intensity (60–70% peak heart rate) with antidepressants is more effective than antidepressant drug therapy alone in elderly patients with MDD. Carneiro et al. [33] corroborate that a supervised program of 16 weeks of generic aerobic exercise (dance, jump and traditional games) in adults with depressive symptoms, performed with controlled intensity (70% HR_{max}), contributes as an adjunct treatment to antidepressant pharmacotherapy

Table 2. Comparison of depressive symptoms between groups (AT, ST and CG) within times (before and after intervention)

	AT (n = 9)		Es		NNT		ST (n = 9)		Es		NNT		CG (n = 7)		Es	NNT	p ¹	p ²	p ³	
	range	mean	range	SD	range	SD	range	mean	range	SD	range	mean	range	mean						range
HAM-D (score)																				
Before	10-18	14.33	2.82	2.82	2.8		7-17	13.44	3.46	1.5		12-17	14.57	1.81	1.3	4,727	0.003*	0.001*	0.014*	
After	5-12	7.44	2.06	2.06	1.8		5-13	8.55	2.87	1.8		11-16	13.42	2.07	6.26 ^a	0.044*	0.044*			
Response HAM-D, n	5	5			1.8		4	2		4.5		0	0		5.71 ^a	0.058				
Remission HAM-D, n	5	5			1.8		4	4		2.3		0	0							
BDI (score)																				
Before	10-28	19.66	6.44	6.44	1.2		11-35	25.56	9.08	1.7		14-24	20.42	3.33	0.9	2,388	0.296	0.001*	0.104	
After	8-18	12.77	3.63	3.63	4.5		5-22	12.88	4.91	1.8		11-22	16.85	3.57	6.26 ^a	0.044*				
Response BDI, n	2	2			4.5		5	5		1.8		0	0							
Remission BDI, n	3	3			3.0		2	2		4.5		0	0		2.77 ^a	0.249				

SD, standard deviation; Es, effect size; NNT, number needed to treat; HAM-D, Hamilton Depression Rating Scale; BDI, Beck's Depression Inventory; AT, aerobic training; ST, strength training; CG, control group (low-intensity exercise/social contact). The variables remission and response rates (HAM-D and BDI) are displayed in frequency. Remission: final HAM-D score ≤ 7 and BDI ≤ 10 . Response: 50% reduction in the pre-post-intervention. Effect size: small (0.2-0.5); medium (0.6-0.8); large (>0.8). Number needed to treat: the optimal NNT value is 1.0. p¹, main effect for group (two-way ANOVA); p², main effect for time (two-way ANOVA); p³, interaction between time and group (two-way ANOVA). * p < 0.05, significant difference. ^a χ^2 value.

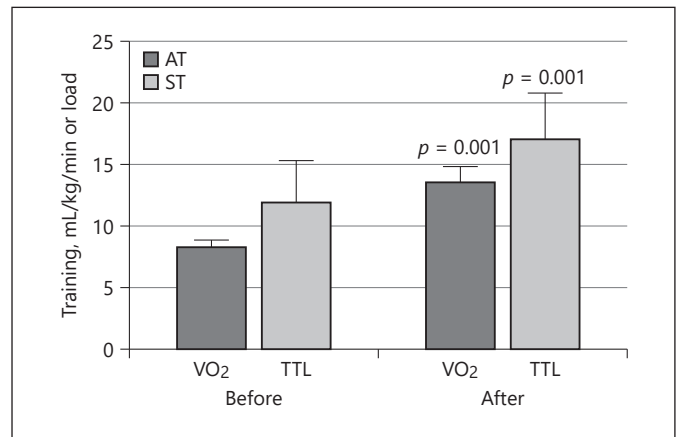


Fig. 2. Compared parameters training before and after intervention (AT and ST groups). AT, aerobic training; ST, strength training; VO₂, American College of Sports Medicine equation oxygen uptake; TTL, total load training. p < 0.05, significant difference (paired-sample t test).

for reducing the symptoms. When studies have compared AT with ST, there are also different findings. Doyné et al. [21] identified a significant reduction in depressive symptoms in adults following 8 weeks of AT (intensity 80% HR) and ST. However, when one study included a control group, they did not find a significant difference between groups [23]. A possible explanation is that relaxation and massage exercise applied in the CG might have an anxiety reduction effect.

In the present study, the CG exhibited no remission and no response to treatment. For this group, low-intensity intervention and nonprogression training were applied. Chalder et al. [34] demonstrated that encouraging choice and autonomy in the adoption of physical activity is not efficient in the reduction of depressive symptoms, possibly because few subjects performed vigorous exercise. In our study, the AT and ST groups exhibited a significant increase in training intensity parameters and a significant decrease in symptoms after intervention. A possible explanation for the efficiency of the two methods may be related to the controlling and maintenance of the intensity parameters. Singh et al. [18] demonstrated a significant relationship between strength gain and reduction of depression symptoms. The authors conclude that 8 weeks of high-intensity training (80% 1RM) were more effective than low-intensity training (20% 1RM) for the treatment of older persons. Martinsen et al. [22] demonstrated that young patients exhibited significantly reduced MDD symptoms after they demonstrated an in-

crease between 15 and 30% $VO_{2\max}$. Dunn et al. [35] concluded that an energy expenditure of 17 kcal/kg/week was more effective in the reduction of MDD symptoms compared with 7 kcal/kg/week, which occurred independently of the weekly frequency (3 or 5 times). In several studies, the interventions had longer durations (8–16 weeks) [15, 24, 35]. However, Knubben et al. [37] reported that AT may promote the reduction of MDD symptoms in a short period of time. Young and elderly patients who added an AT routine (80% HR_{\max}) to pharmacological treatment for 10 consecutive days achieved a higher response rate to treatment (65%) than the group that received medication therapy (22%).

Another interesting finding in the present study is the NNT found. The AT and ST groups presented an NNT of 1.8, as assessed by the HAM-D and BDI scales, when compared to the CG. This means that, each rough fully 2 patients treated, one will present additional remission at the end of the trial when compared to the CG. This rate is lower than found in Schuch et al. [38] (NNT = 6.25) and Trivedi et al. [39] (NNT = 7.8). Several neurophysiological mechanisms have been proposed to explain this outcome. A review regarding the effect of exercise on mental health indicates that neurobiological alterations may contribute to the improved response to treatment [9].

Based on these results, one can interpret that regular physical activity has clinical benefits for seniors diagnosed with MDD. People with mental illness have an increased risk of physical disease, as well as reduced access to adequate care. Consequently, physical exercise is an additional treatment to reduce costs of physical comorbidities [39]. In clinical applications, the two training methods applied during the same session may increase the likelihood of a treatment response [40, 41]. However, it is necessary to determine the intensity and the training method to optimize treatment efficiency. A 2–3 times a week exercise routine (AT or ST) with 30-min moderate intensity (70–85% HR_{\max}) has shown to be effective in reducing MDD symptoms in many studies. We also note that future research should investigate different methods and training intensities. In addition to mental health benefits, the 12 weeks of intervention provided an increase in strength and cardiopulmonary capacity in older persons. These results may be associated with other health benefits, such as improvement of the immune system, increase in bone density, maintenance of muscle mass, control of body weight, low blood glucose levels, and reduced risk of death from cardiovascular diseases [42]. Moreover, a previous study observed increased serum insulin-like

growth factor 1 levels in a group of elderly individuals after 6 months of ST [16]. Insulin-like growth factor 1 has a protective and restoring effect on the brain and also modulates neuronal plasticity.

This study has some limitations: (1) small sample size; although we have found significant results, a bigger sample promotes more robust findings; (2) the indirect lack of cardiovascular fitness evaluation after intervention; this variable could contribute to the association between cardiovascular improvement and depression reduction; however, both groups increased their training parameters, which is suggestive of an increase in cardiovascular fitness; (3) the exclusion of patients with severe depression symptoms. Thus, we consider that the outcomes of this study can only be generalized for older people with light MDD, but not to people with moderate to severe episodes. A strength of this study is that the patient adherence has favored the maintenance of groups by the end of training. This may provide indirect evidence of the feasibility of a regular exercise protocol in clinical settings. Furthermore, this is to the best of our knowledge the first clinical trial to compare AT and ST in older people with MDD with a favorable outcome. Future studies could reply to this methodology including follow-up examination. In conclusion, both strength and aerobic training combined with pharmacological treatment can contribute to an improved treatment response in elderly patients who suffer from MDD.

Acknowledgments

This study was supported by grants from Conselho Nacional Desenvolvimento e Tecnológico (CNPq) during the design and conduct of the survey and from Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

Statement of Ethics

All subjects have given their written informed consent. The research respected the ethical principles established by the Declaration of Helsinki and was registered in 2014 in the Brazilian Clinical Trials (ReBec) (register No. RBR-38nkj6). It was also approved in 2009 (register No. 007-09-CEP) by the Ethics Committee of the Institute of Neurology Deolindo Couto (INDC) of the Federal University of Rio de Janeiro (UFRJ).

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study was supported by grants from Conselho Nacional Desenvolvimento e Tecnológico (CNPq) during the design and conduct of the survey and from Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

Author Contributions

Helena S. Moraes – has written the paper and interpretation of the results. Heitor S. Silveira – acquisition and analysis of the data. Natacha A. Oliveira – acquisition of the data. Eduardo M. Portugal – analysis of the data. Narahyana B. Araújo – acquisition of the data. Paulo A. Vasques – revision of the paper. Astrid Bergland – revision of the paper. Tony M. Santos – analysis of the data and revision of the paper. Knut Engedal – revision of the paper. Evandro S. Coutinho – interpretation of the results and statistical analysis. Felipe B. Schuch – interpretation of the results and revision the paper. Jerson Laks – drafting the work. Andrea C. Deslandes – drafting the work and revision of the paper.

References

- 1 Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, et al.; STAR*D Study Team. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. *Am J Psychiatry*. 2006 Jan; 163(1):28–40.
- 2 Greden JF. Unmet need: what justifies the search for a new antidepressant? *J Clin Psychiatry*. 2002;63 Suppl 2:3–7.
- 3 Anderson IM. Selective serotonin reuptake inhibitors versus tricyclic antidepressants: a meta-analysis of efficacy and tolerability. *J Affect Disord*. 2000 Apr;58(1):19–36.
- 4 Byers AL, Vittinghoff E, Lui LY, Hoang T, Blazer DG, Covinsky KE, et al. Twenty-year depressive trajectories among older women. *Arch Gen Psychiatry*. 2012 Oct;69(10):1073–9.
- 5 Stubbs B. A meta-analysis investigating falls in older adults taking selective serotonin reuptake inhibitors confirms an association but by no means implies causation. *Am J Geriatr Psychiatry*. 2015 Oct;23(10):1098.
- 6 Coupland C, Dhiman P, Morriss R, Arthur A, Barton G, Hippisley-Cox J. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. *BMJ*. 2011 Aug 2;343:d4551.
- 7 Greist JH, Klein MH, Eischens RR, Faris J, Gurman AS, Morgan WP. Running as treatment for depression. *Compr Psychiatry*. 1979 Jan-Feb;20(1):41–54.
- 8 Klein MH, Greist JH, Gurman AS, Neimeyer RA, Lesser DP, Bushnell NJ Sr. A comparative outcome study of group psychotherapy vs. exercise treatments for depression. *Psychother Depress*. 1985;13:148–76.
- 9 Deslandes A, Moraes H, Ferreira C, Veiga H, Silveira H, Mouta R, et al. Exercise and mental health: many reasons to move. *Neuropsychobiology*. 2009;59(4):191–8.
- 10 Singh NA, Clements KM, Singh MA. The efficacy of exercise as a long-term antidepressant in elderly subjects: a randomized, controlled trial. *J Gerontol A Biol Sci Med Sci*. 2001 Aug;56(8):M497–504.
- 11 Lawlor DA, Hopker SW. The effectiveness of exercise as an intervention in the management of depression: systematic review and meta-regression analysis of randomised controlled trials. *BMJ*. 2001 Mar;322(7289):763–7.
- 12 Cooney G, Dwan K, Mead G, Lawlor DA, Rimer J, Waugh FR, et al. Exercise for depression. *JAMA*. 2014 Jun;311(23):2432–3.
- 13 Rethorst CD, Wipfli BM, Landers DM. The antidepressive effects of exercise: a meta-analysis of randomized trials. *Sports Med*. 2009; 39(6):491–511.
- 14 Schuch FB, Vancampfort D, Rosenbaum S, Richards J, Ward PB, Veronese N, et al. Exercise for depression in older adults: a meta-analysis of randomized controlled trials adjusting for publication bias. *Br J Psychiatry*. 2016 Jul-Sep;38(3):247–54.
- 15 Blumenthal JA, Babyak MA, Doraiswamy PM, Watkins L, Hoffman BM, Barbour KA, et al. Exercise and pharmacotherapy in the treatment of major depressive disorder. *Psychosom Med*. 2007 Sep-Oct;69(7):587–96.
- 16 Cassilhas RC, Viana VA, Grassmann V, Santos RT, Santos RF, Tufik S, et al. The impact of resistance exercise on the cognitive function of the elderly. *Med Sci Sports Exerc*. 2007 Aug;39(8):1401–7.
- 17 Silveira H, Moraes H, Oliveira N, Coutinho ES, Laks J, Deslandes A. Physical exercise and clinically depressed patients: a systematic review and meta-analysis. *Neuropsychobiology*. 2013;67(2):61–8.
- 18 Singh NA, Stavrinou TM, Scarbek Y, Galambos G, Liber C, Singh MAF, et al. A randomized controlled trial of high versus low intensity weight training versus general practitioner care for clinical depression in older adults. *J Gerontol A Biol Sci Med Sci*. 2005;60(6):768–76.
- 19 Krogh J, Nordentoft M, Sterne JA, Lawlor DA. The effect of exercise in clinically depressed adults: systematic review and meta-analysis of randomized controlled trials. *J Clin Psychiatry*. 2011 Apr;72(4):529–38.
- 20 Krogh J, Hjorthøj C, Speyer H, Gluud C, Nordentoft M. Exercise for patients with major depression: a systematic review with meta-analysis and trial sequential analysis. *BMJ Open*. 2017 Sep;7(9):e014820.
- 21 Doynne EJ, Ossip-Klein DJ, Bowman ED, Osborn KM, McDougall-Wilson IB, Neimeyer RA. Running versus weight lifting in the treatment of depression. *J Consult Clin Psychol*. 1987 Oct;55(5):748–54.
- 22 Martinsen EW, Hoffart A, Solberg O. Comparing aerobic with nonaerobic forms of exercise in the treatment of clinical depression: a randomized trial. *Compr Psychiatry*. 1989 Jul-Aug;30(4):324–31.
- 23 Krogh J, Saltin B, Gluud C, Nordentoft M. The DEMO trial: a randomized, parallel-group, observer-blinded clinical trial of strength versus aerobic versus relaxation training for patients with mild to moderate depression. *J Clin Psychiatry*. 2009 Jun;70(6):790–800.
- 24 Cohen J. The earth is round ($p < 0.05$). *Am Psychol*. 2004;49(12):997–1003.
- 25 Firth J, Rosenbaum S, Stubbs B, Gorkzynski P, Yung AR, Vancampfort D. Motivating factors and barriers towards exercise in severe mental illness: a systematic review and meta-analysis. *Psychol Med*. 2016;46:2869–81.
- 26 Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960 Feb; 23(1):56–62.
- 27 Folstein MF, Folstein SE, McHugh PR. Minimal state. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189–98.
- 28 Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961 Jun;4(6):561–71.
- 29 Borg G. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 1982;14(5):377–81.
- 30 Laupacis A, Sackett DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. *N Engl J Med*. 1988 Jun;318(26):1728–33.
- 31 Krogh J, Videbeck P, Thomsen C, Gluud C, Nordentoft M. DEMO-II trial. Aerobic exercise versus stretching exercise in patients with major depression—a randomised clinical trial. *PLoS One*. 2012;7(10):e48316.

- 32 Belvederi Murri M, Amore M, Menchetti M, Toni G, Neviani F, Cerri M, et al.; Safety and Efficacy of Exercise for Depression in Seniors (SEEDS) Study Group. Physical exercise for late-life major depression. *Br J Psychiatry*. 2015 Sep;207(3):235–42.
- 33 Carneiro LS, Fonseca AM, Vieira-Coelho MA, Mota MP, Vasconcelos-Raposo J. Effects of structured exercise and pharmacotherapy vs. pharmacotherapy for adults with depressive symptoms: a randomized clinical trial. *J Psychiatr Res*. 2015 Dec;71:48–55.
- 34 Chalder M, Wiles NJ, Campbell J, Hollinghurst SP, Searle A, Haase AM, et al. A pragmatic randomised controlled trial to evaluate the cost-effectiveness of a physical activity intervention as a treatment for depression: the treating depression with physical activity (TREAD) trial. *Health Technol Assess*. 2012; 16:1–164.
- 35 Dunn AL, Trivedi MH, Kampert JB, Clark CG, Chambliss HO. Exercise treatment for depression: efficacy and dose response. *Am J Prev Med*. 2005 Jan;28(1):1–8.
- 36 Deslandes AC, Moraes H, Alves H, Pompeu FA, Silveira H, Mouta R, et al. Effect of aerobic training on EEG alpha asymmetry and depressive symptoms in the elderly: a 1-year follow-up study. *Braz J Med Biol Res*. 2010 Jun; 43(6):585–92.
- 37 Knubben K, Reischies FM, Adli M, Schlattmann P, Bauer M, Dimeo F, et al. A randomised, controlled study on the effects of a short-term endurance training programme in patients with major depression. *Br J Sports Med*. 2007 Jan;41(1):29–33.
- 38 Schuch FB, Vasconcelos-Moreno MP, Borowsky C, Zimmermann AB, Rocha NS, Fleck MP. Exercise and severe major depression: effect on symptom severity and quality of life at discharge in an inpatient cohort. *J Psychiatr Res*. 2015 Feb;61:25–32.
- 39 Trivedi MH, Greer TL, Church TS, Carmody TJ, Grannemann BD, Galper DI, et al. Exercise as an augmentation treatment for nonremitted major depressive disorder: a randomized, parallel dose comparison. *J Clin Psychiatry*. 2011 May;72(5):677–84.
- 40 Silveira H, Deslandes AC, de Moraes H, Mouta R, Ribeiro P, Piedade R, et al. Effects of exercise on electroencephalographic mean frequency in depressed elderly subjects. *Neuropsychobiology*. 2010;61(3): 141–7.
- 41 Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, Minson CT, Nigg CR, Salem GJ, et al.; American College of Sports Medicine. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc*. 2009 Jul; 41(7):1510–30.
- 42 Singh NA, Clements KM, Fiatarone MA. A randomized controlled trial of progressive resistance training in depressed elders. *J Gerontol A Biol Sci Med Sci*. 1997 Jan;52(1):M27–35.