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ORIGINAL RESEARCH

Aerobic exercise reduces anxiety symptoms and improves fitness in patients with panic disorder

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OBJECTIVE: To investigate the effects of a regularly repeated aerobic exercise series on anxiety and maximum oxygen consumption (VO_{2max}) in Panic Disorder patients.
METHODS: Ten previously sedentary female subjects diagnosed with Panic Disorder performed 36 sessions of aerobic exercise (at 70 to 75% of VO_{2max}), 3 times per week during 12 weeks. A cardiopulmonary evaluation (ergospirometry test) was used to set the intensity of training as well as to establish baseline and post-training VO_{2max} parameters. The assessment of anxiety symptoms was performed at baseline, at the end of the 6th and 12th weeks, using the Trait Anxiety Inventory (STAI-T) and State Anxiety Inventory (STAI-S), and the Subjective Units of Distress Scale (SUDS) questionnaires. One-way ANOVA for repeated measurements (at 3 moments: Baseline, 6th week (mid-training) and 12th week (post-training) was used to compare the evolution of the questionnaires; the Bonferroni *post hoc* test was applied to identify differences between moments. A dependent t-test was performed for measures of VO_{2max}.
RESULTS: Compared to baseline, (a) STAI-T showed significant anxiety reductions at mid- and post-training moments; (b) STAI-S and SUDS recorded anxiety reductions only at Post-training; (c) VO_{2max} showed a significant improvement at Post-training.
CONCLUSION: This protocol promoted beneficial effects on cardiorespiratory fitness and anxiety levels of Panic Disorder patients.

KEYWORDS: Panic disorder, aerobic exercise, maximum oxygen consumption.

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INTRODUCTION

Panic disorder (PD) consists of recurrent unexpected panic attacks**,** followed by persistent concerns about the recurrence of other crises and their consequences.[1] Such patients are effectively treated using drugs or cognitive behavioral therapy, with the aim of reducing symptoms of anxiety and decreasing the frequency of panic attacks.[2,3] However, as much as the use of drugs such as benzodiazepines or specific antidepressants (tricyclic compounds and Selective Serotonin Reuptake Inhibitors) have shown efficacy for decades,[4-6] side effects are commonly reported, with significant impairment to different cognitive domains, associated to prolonged use of certain drugs;[7] these facts suggest the need for different treatment strategies.

Exercise is increasingly regarded as a therapeutic intervention for patients with different psychiatric disorders, due to its vast benefits on physical and mental health.[8-12] A recent study showed significant anxiolytic and antidepressant effects resulting from regular physical exercise.[13] Gaudlitz et al.[14] demonstrated that aerobic

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exercise (AE) associated with cognitive behavioral therapy promotes additional benefits in terms of decreasing anxiety levels. It has also been shown that the performance of AE, preceding a provocative test of CO_2 inhalation, results in a significant reduction in the anxiogenic responses compared with subjects rested before the test.[15] It has also been reported that aerobic exercise, performed on the treadmill, at 70% of VO_{2max} for 30 minutes, had a positive effect on the reduction in anxiety levels and in the frequency of panic attacks in PD patients after a provocative test with cholecystokinin.[16]

Nevertheless, there is still great opposition to the inclusion of exercise as a treatment for PD. A meta-analysis published by Bartley et al.[17] demonstrated that there is no evidence to support the use of AE as an effective treatment for anxiety disorders when compared to control conditions. This study reveals no positive effect of AE for different types of anxiety disorder. In addition, physical exercise may induce panic attacks,[18,19] causing an increase in exercise avoidance by these PD patients.[20]

Thus, the aim of this study was to investigate the effects of continuous AE on anxiety and VO_{2max} in PD patients. We hypothesized that in the end of the training period there would be a significant improvement of anxiety and of VO_{2max}.

METHODS

Subjects

The sample was composed of ten inactive female subjects. They were invited to participate in the study on a voluntary basis and signed an informed consent term. The following criteria for inclusion were adopted: patients (a) with a diagnosis of PD;1 (b) with negative responses in a physical activity readiness questionnaire; (c) who had not performed AE regularly for at least six months. The exclusion criteria were: patients (a) with cardiovascular disease; (b) with arterial blood pressure ≥ 140x90 mmHg; (c) with musculoskeletal impairment. (d) who have not completed twelve weeks of aerobic exercise (36 sessions). Table 1 shows the general features of the included patients.

Table 1 - Sample characterization (n = 10)

Features	Mean ± SD
Age (years)	43,3 ± 10,75
Weight (kg)	59,0 ± 11,5
Height (cm)	162 ± 6,6
Fat Percentage (%)	17,0 ± 4,2
$V0_{2max}$ ($ml.kg.^{-1}$ $min.^{-1}$)	22,5 ± 8,8
Medication	CL, PP, CT, AL, VF, FH
Years of Education	(13 ± 2,2)

Subtitles: SD = Standard deviation; CL = clonazepam; PP = propanolan; CT = citalopran; AL = alprazolan; VF = Venlafaxine; FH = Fluoxetine-hydrochloride.

During the 12 weeks of the study, the subjects received specific guidelines for: (a) the use specific clothing and shoes for the practice of exercise and (b) to consume no alcohol or stimulants (coffee, tea, chocolate) 24 hours before exercise sessions. Throughout the study the subjects used the following drugs: clonazepam, propanolan, citalopran, alprazolan, venlafaxine; fluoxetine-hydrochloride. Patients were asked to report any decreases or increases in the number or dose of any drug. In all exercise sessions, professionals involved in the data acquisition sought to motivate patients and to maintain regular contact via email to make them aware of the time of exercise sessions, as an effort to avoid dropouts. This study was approved by Institutional Ethics Committee of Universidade Salgado de Oliveira, case # 875.986.

Experimental Procedure

The study was conducted in three phases: (1) baseline assessment; (2) experimental procedure: 36 sessions of AE; (3) reassessment.

Baseline evaluation was conducted during two sessions: Session #1: measurement of resting heart rate, collection of anthropometric features, familiarization with treadmill running, and with cardiorespiratory test; Session #2) a new cardiorespiratory test, and ministration of anxiety scale questionnaires.

During the experimental phase, patients performed 36 sessions of continuous AE at 70-75% VO_{2max}. At the 6th week, the anxiety scales were re-applied. At the end of the experimental phase (i.e., 12th week), a new cardiorespiratory test and the anxiety scales were applied. All the tests and the sessions of aerobic exercise were conducted in an air-conditioned closed environment (20° - 21°C). A 48-hour rest interval was allowed between sessions. Figure 1 is a schematic representation of the timeline of this study.

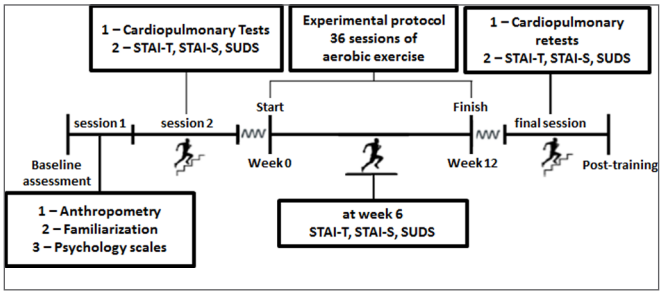

Figure 1 - Schematic representation of the experimental timeline. The protocol comprised three phases: baseline assessment (2 sessions), experimental procedure (36 sessions), reassessment (1 session).

Cardiorespiratory Test

All participants performed an individual protocol with an average estimated duration of 10 min.[21] The test was performed at a constant gradient of 1% and began with 50% of the predicted VO_{2max} value.[22] The speed increase ratio was 0.8 $km.h^{-1}$ imposed at 1-minute intervals until exhaustion. The respiratory and gas exchange were measured using

a computerized ergospirometric analysis with VO_{2000} device (CPX-D *Medical Graphics TM*, Saint Paul, MN, USA), calibrated according to factory specifications. Heart rate was monitored by a Polar heart monitor (model RS_{800}), recorded at every minute until exhaustion, and five minutes after the end of the test. The maximum voluntary exhaustion, as well as any signs or symptoms mentioned or presented by the patients ware used as criteria for test termination.

Anxiety Scales - STAI and SUDS

The anxiety scales were applied in three phases: baseline, sixth week, and post-training (i.e., after 12 weeks).

STAI is composed of two subscales: a) STAI-T which aims to evaluate traits of anxiety; b) STAI-S which aims to evaluate a state of anxiety. Both scales contain 20 items.[23] The instrument is a self-report scale (i.e., a "Likert" type scale) with scores ranging from 1 ("almost never") a 4 ("almost always"). The total scores range from 20 to 80.

The SUDS scale describes the magnitude of the provocative stimulus of the fear/anxiety response. It ranges from 0 to 100 points. Briefly, ratings are as follow: 0 - absent; 10-20 - minimum; 30-40 - average; 50-60 - moderate; 70-80 - high; 90-100 - maximum. Details have been described elsewhere.[24,25]

Aerobic Exercise Sessions

All subjects performed the training routine without interruptions and in the same calibrated treadmill. For all of the 36 sessions, subjects were positioned on the treadmill and received information about the training procedures; they were encouraged to work until the end of the set time, but advised that they could also abort the training session to signal complications or fatigue. The intensity settings occurred at 40-45% for warm up, 70-75% VO_{2max} for training and 40-45% for cool down.

Statistical Analysis

Results are shown as average ± standard deviation. Preliminarily the normality of distribution, and the variance of the data was checked. An ANOVA one-way repeated measurements test was performed for baseline, sixth week, and post-trainings; to compare the dependent variables (STAI-T, STAI-S, SUDS). A Bonferroni *post hoc* test was applied to identify differences between moments. For measures of VO_{2max} a dependent *t-test* (pre-post) was performed. All analysis were performed by means of the statistical pack SPSS 20.0; a level of significance $p < 0.05$ was adopted.

RESULTS

The study initially included 14 women, but four did not complete all the AE sessions (12 weeks). Ten women completed all AE exercise sessions. The results show the main effects for moment (i.e., baseline, sixth week and post-training) for STAI-T ($F(2) = 16\,738$; $p < 0.001$), STAI-S ($F(2) = 4.554$; $p = 0.02$) and SUDS ($F(2) = 4963$; $p = 0.018$): significant reductions were observed for all the three scales. The post-hoc Bonferroni test showed (a) for STAI-T there are significant decreases from control to the 6th week and to end of training (mean: 57.3, SD: 8.7) compared to 6th week (mean: 51.7, SD: 10.2; $p = 0.006$) and at post-training (12th week; mean: 44.2, SD: 10.2; $p = 0.02$). (b), for STAI-S and for SUDS reductions were only significant between control and after 12 weeks of exercise (mean: 34.4, SD: 5.8; $p = 0.01$) and (mean: 12, SD: 16; $p = 0.03$) compared to baseline (STAI-S, mean: 42.0, SD: 9.0; SUDS, mean: 27, SD: 16), respectively (Figure 2).

VO_{2max} showed a significant improvement after the intervention (Post-training = 24.2 ± 9.2 ml.kg-1.min-1 vs. Baseline = 22.5 ± 8.8 ml.kg-1.min-1) This increase was significant according to Student's "t" test ($t = -2.61$; $p = 0:02$).

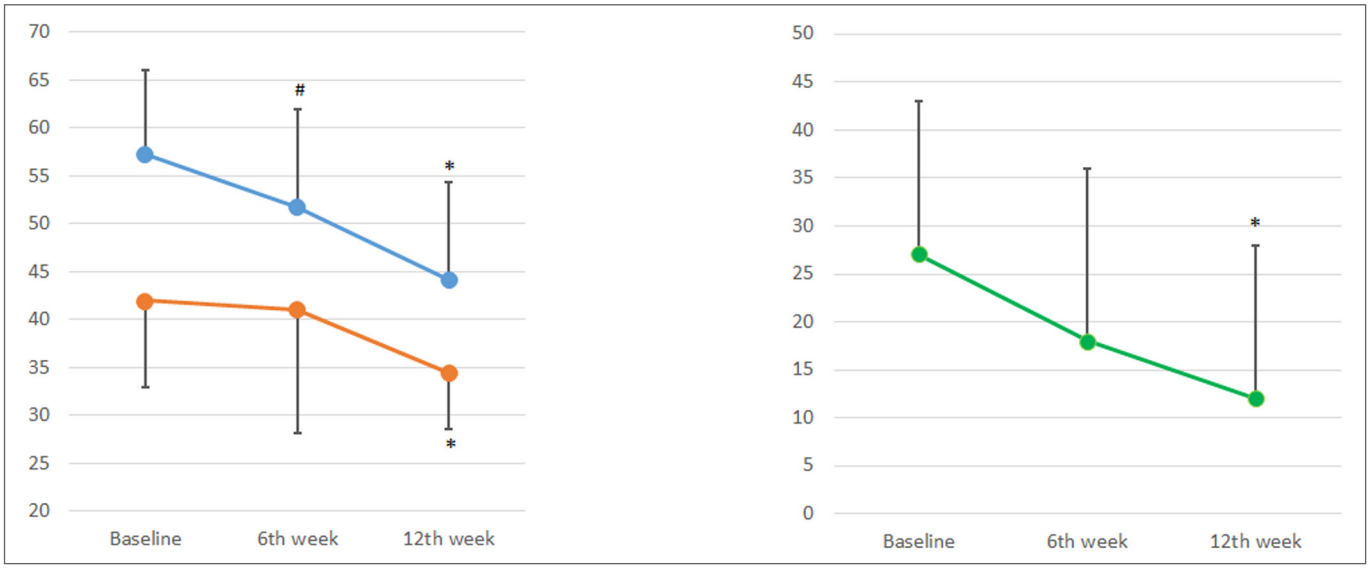

Figure 2 - Behavior of indicators STAI-T, STAI-S and SUDS (M ± SD) at Baseline, at week 6, at Post Training. * Baseline vs Post Training: $p < 0.05$; # Baseline vs Sixth week ($p < 0.05$).

DISCUSSION

The aim of this study was to investigate the effects of regularly repeated aerobic exercise (AE) on anxiety levels and on maximal oxygen consumption (VO_{2max}) in individuals with panic disorder (PD). Our results indicate an improvement in anxiety symptoms and an increase of VO_{2max}.

Some controlled studies that investigated the chronic effects of AE on anxiety levels of PD patients reported conflicting results.[26,18,19,27,28]

A number of reports claim that AE compared to other forms of treatment was not effective in reducing anxiety symptoms in PD patients.[18,26,28,29] Medication has been reported to be the most effective treatment,[18,26,29] while cognitive behavioral therapy was also described as effective.[28] In a meta-analysis published by Bartley et al.[15] evidence did not support the use of AE as an effective treatment for PD patients. Merom et al.[27] reported that a cognitive behavioral therapy intervention associated with exercise (compared with a cognitive behavioral therapy intervention associated with educational programs) did not result in the improvement of stress, anxiety and depression in PD patients. Perhaps, the lack of a structured protocol prescription of AE may have influenced these results.

In contrast to these reports, Gaudlitz et al.[14] demonstrated that AE (i.e., 30 minutes at 70% VO_{2max}, 3 times a week) associated with cognitive behavioral therapy resulted in a reduction of anxiety levels. AE performed in another study, (six sessions of 20 minutes at 70% maximum heart rate) also decreased the anxiety sensitivity compared to unexercised controls.[30] It should be noted that AE provokes an increase in atrial natriuretic peptide levels (known to induce anxiolytic effects) and a reduction in panic symptoms.[16,31] Meyer et al.[18] also showed that PD patients who performed AE for ten weeks, compared to an non-exercised control group, presented reductions in anxiety scores in the 6th and 10th weeks. Lambert et al.[32] sought to analyze the effects of free exercises and occupational therapy on anxiety as a measure of treatment for PD in patients with moderate to severe anxiety. Their results showed a significant decrease in anxiety levels in the experimental group compared to the control group. In addition, patients had fewer panic attacks up to 20 weeks after the intervention period. They concluded that a healthy lifestyle can be effective in significantly reducing anxiety.[32]

Furthermore, the regular practice of AE can provide improvements in cardiorespiratory fitness of these patients. Corroborating our findings, Martinsen et al.[33] reported the results of a protocol of 1 hour of AE at 70% VO_{2max}, 3 times a week for 8 weeks, in which they observed a significant increase in VO_{2max} with significant reductions in the anxiety levels.

Medication is clearly an effective controlling agent for PD, but side effects should be taken into account, especially because exercise does not provoke side effects; thus, it should be regarded as a potential additional non-pharmacological therapy for PD.

Thus, it appears that the adoption of an AE program can be a useful tool to promote benefits related to health of PD individuals, considering that an increase in cardiorespiratory fitness is related positively to improved life expectancy.

LIMITATIONS

It is important to address some limitations of our study. First, the small number of participants; second, the lack of a control group; third, the lack of a follow-up assessment.

CONCLUSION

We conclude that the adopted protocol was able to promote beneficial effects on cardiorespiratory fitness and anxiety levels of Panic Disorder (PD) patients: aerobic exercise may be a potential non-pharmacological therapy to reduce anxiety symptoms in these patients. Further studies are necessary to investigate other protocols with different parameters in order to increase information about a precise aerobic exercise prescription for PD.

CONFLICT OF INTEREST

The authors state no conflict of interest regarding this project.

AUTHOR PARTICIPATION

Lamego MK, Lattari E, de Sá Filho AS, Paes F, Maranhão Neto G, de Oliveira AJ, Campos C, Rocha NBF, Nardi AE, Machado S reviewed the literature and the final version of the article. Mascarenhas Jr. J, Machado S developed the project, contributed in work orientation, discussed the data, wrote the first draft of the article.

EXERCÍCIOS AERÓBICOS REDUZIRAM OS SINTOMAS DE ANSIEDADE E MELHORARAM O DESEMPENHO CARDIORRESPIRATÓRIO EM PORTADORES DE TRANSTORNO DE PÂNICO

OBJETIVO: O objetivo deste estudo foi investigar os efeitos do exercício aeróbio praticado regularmente sobre a ansiedade e o VO_{2max} em pacientes com transtorno de pânico.

MÉTODO: Dez mulheres sedentárias diagnosticadas com transtorno de pânico (TP) realizaram 36 sessões de exercícios aeróbico contínuo (70 a 75% VO_{2max}) em esteira, 3x por semana, durante 12 semanas. Uma avaliação cardiopulmonar (teste ergo-espirométrico) definiu a intensidade do treinamento, bem como estabeleceu valores de VO_{2max} pré e pós-treinamento. A avaliação dos sintomas de ansiedade nos três momentos (controle, 6° e 12° semana), foi realizada utilizando os questionários IDATE-T (Inventário do Traço de Ansiedade), IDATE-S (Inventário do Estado de Ansiedade) e SUDS (Unidades Subjetivas da Escala de Aflição). O teste ANOVA One-way para medidas repetidas (momentos) foi usado para comparar os questionários. O teste Bonferroni post-hoc foi aplicado para identificar as diferenças entre os momentos. As medidas de VO_{2max} foram analisadas através de um teste de "t" dependente.

RESULTADOS: Os resultados mostraram redução do IDATE-T na 6° e 12° semanas de exercício; no entanto, o IDATE-S e o SUDS monstraram uma redução apenas na 12° semana. O VO_{2max} apresentou melhora significativa após 12 semanas de intervenção em relação à linha de base.

CONCLUSÃO: Conclui-se que o protocolo adotado foi capaz de promover efeitos benéficos sobre a aptidão cardiorrespiratória e sobre os níveis de ansiedade dos pacientes com transtorno de pânico.

PALAVRAS-CHAVE: Transtorno de Pânico, Exercício aeróbico, VO_{2max}.

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