Effects of Aerobic Exercise on Anxiety Disorders: A Systematic Review

Antonio Marcos de Souza Moura, Murilo Khede Lamego, Flávia Paes, Nuno Barbosa Ferreira Rocha, Vitor Simões-Silva, Susana Almeida Rocha, Alberto Souza de Sá Filho, Ridson Rimes, João Manochio, Henning Budde, Mirko Wegner, Gioia Mura, Oscar Arias-Carrión, Ti-Fei Yuan, Antonio Egidio Nardi and Sergio Machado

Abstract: Anxiety disorders are the most common psychiatric disorders observed currently. It is a normal adaptive response to stress that allows coping with adverse situations. Nevertheless, when anxiety becomes excessive or disproportional in relation to the situation that evokes it or when there is not any special object directed at it, such as an irrational dread of routine stimuli, it becomes a disabling disorder and is considered to be pathological. The traditional treatment used is medication and cognitive behavioral psychotherapy, however, last years the practice of physical exercise, specifically aerobic exercise, has been investigated as a new non-pharmacological therapy for anxiety disorders. Thus, the aim of this article was to provide information on research results and key chains related to the therapeutic effects of aerobic exercise compared with other types of interventions to treat anxiety, which may become a useful clinical application in a near future. Researches have shown the effectiveness of alternative treatments, such as physical exercise, minimizing high financial costs and minimizing side effects. The sample analyzed, 66.8% was composed of women and 80% with severity of symptoms anxiety as moderate to severe. The data analyzed in this review allows us to claim that alternative therapies like exercise are effective in controlling and reducing symptoms, as 91% of anxiety disorders surveys have shown effective results in treating. However, there is still disagreement regarding the effect of exercise compared to the use of antidepressant symptoms and cognitive function in anxiety, this suggests that there is no consensus on the correct intensity of aerobic exercise as to achieve the best dose-response, with intensities high to moderate or moderate to mild.

Keywords: Anxiety, aerobic exercise, cognitive functions.

INTRODUCTION Anxiety disorders are the most common psychiatric disorders observed currently. It is a normal adaptive response to stress that allows coping with adverse situations [1,2]. Nevertheless, when anxiety becomes excessive or disproportional in relation to the situation that evokes it or when there is not any special object directed at it, such as an irrational dread of routine stimuli, it becomes a disabling disorder and is considered to be pathological [1]. The traditional treatment used is medication and cognitive behavioral psychotherapy [3], however, last years the practice of physical exercise, specifically aerobic exercise, has been investigated as a new non-pharmacological therapy for anxiety disorders. It is well-described in the literature that aerobic exercise can bring great benefits to physical health, such as improvement in cardiorespiratory fitness, reduction in blood pressure and body fat, as well as mental health, as the intensity of negative thoughts and the improvement in wellbeing, mood and anxiety [4], with the advantage of do not generate side effects [5, 6]. Therefore, aerobic exercise has been considered a promising intervention strategy as a treatment to reduce anxiety symptoms [7-10], with numerous benefits to physical and mental health, as well as lower cost. However, there are still differences regarding the effects of exercise compared to

pharmacological effects in anxiety symptoms. These findings suggest that there is still not a consensus on the correct aerobic exercise intensity so that the best dose-response can be found, with mild to moderate or moderate to high intensities [11]. Thus, this review paper aims to provide information on the current research and main findings related to the potential therapeutic effects of aerobic exercise compared to other types of interventions to treat anxiety that can become viable as clinical applications in the coming years.

MATERIALS AND METHODS

Eligibility Criteria

The structuring of the methods of the present study will follow the proposals of PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) [12]. Thus, PICOS ("population", "intervention", "compared to control groups", "outcomes" and "study design") [12] approach will be adopted for the determination of eligibility.

1. Population - young adults, men and/or women, physically active or not, with a diagnosis of any anxiety disorder, aged between 18 and 60 years;

2. Intervention – patients must perform any type of aerobic exercise;

3. Comparators - aerobic exercise compared to antidepressants or benzodiazepines, others types of exercise, psychotherapy, psychoeducation, alternative therapy;

4. Outcomes - Symptoms and cognitive functions will be analyzed by scales/inventories of subjective symptoms of anxiety and neuropsychological tests.

5. Study Design - randomized clinical trials that assessed the chronic effect of aerobic exercise on anxiety

Sources of Information

For gathering of studies the electronic databases MEDLINE / PubMed, ISI Web of Knowledge and SciELO were accessed. Experts on the subject of the present study were also contacted to send articles. To find additional articles, all tables were examined for evidence of previous systematic reviews and searched the references of randomized and controlled clinical trials when required.

Furthermore, also references of all selected articles were analyzed. The search was closed on the day 20 June 2014.

Search

In all databases were made the combinations of the terms: aerobic exercise AND disorders OR cognitive functions.

Selection of Studies

The selection of the studies was carried out by two independent assessors, which in case of divergences have sought a consensus on the selection. The evaluation consisted in the filtering of the studies, starting with the analysis of the title, followed by the analyses of the abstract and after the analysis of the full article. In need to solve possible disagreements between the two evaluators, one third evaluator was requested for the due order. Complete relevant articles were obtained and evaluated with inclusion and exclusion criteria, described below.

Data Collection

The following data were extracted from the articles: sample size, participant characteristics, type of exercise, setting of the exercises (intensity, duration of exercise and total length), scales/inventories used, and main significant results. In addition several other information about the methods and outcomes were collected. These procedures done by two independent investigators, who reached a consensus, were performed in case of divergence.

Exclusion Criteria

Were excluded Articles that had no effective exercise intervention; those used otherwise associated with physical exercise that could create a risk of bias in the study, composite samples of the elderly, children and adolescents intervention; individuals with neurological disease; those who did not have detailed statistical procedure applied; studies assessing only the experimental group without a control group or did not show the results of varying symptomatology and cognitive functions.

Risk of Bias in Studies

For assessing the risk of bias of each article included, were analyzed: the presence of the eligibility criteria for participants in the sample; randomization of participants, the results of every moment from the analysis of more than 85% of the sample, the presence of the control group, presentation of results and intergroup variability of results.

RESULTS

Based on the defined criteria, a total of 77 articles were found in the search conducted in the literature. Of these, 7 articles were duplicates and were therefore excluded, totalizing 70 articles. After the screening, 60 articles were excluded, which were not related to the proposed theme. 10 articles remained, and after new screening, any article was

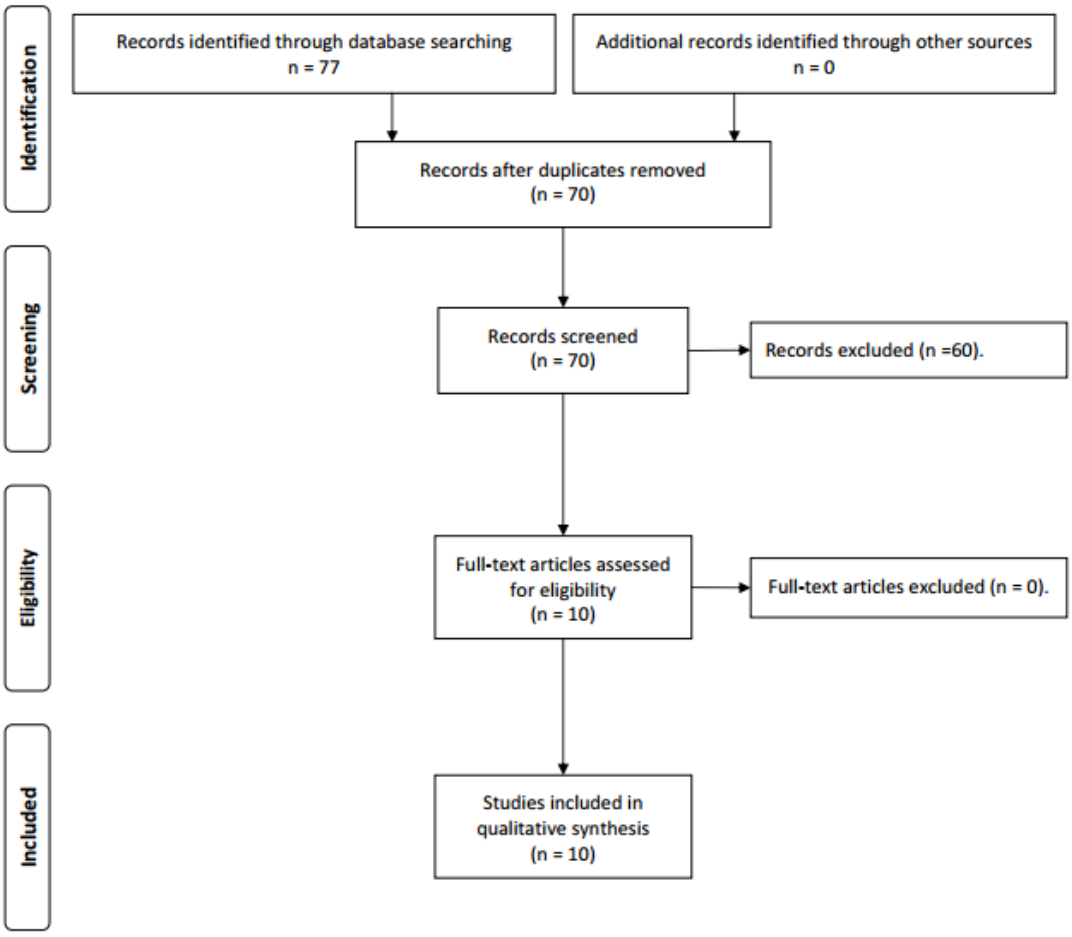

Fig. (1). Flow chart for the articles included in the systematic review.

excluded (see Fig. 1). Thus, studies were selected which properly met the criteria for this review. We found 10 studies about anxiety (Table 1). The sample analyzed, 33.2% was composed of men and 66.8% of women, as the severity of symptoms 20% had mild to moderate anxiety and 80% had moderate to severe anxiety. Assessment of risk of bias revealed that all articles selected met just one criteria. The majority of the articles have not results from 85% of sample (Table 2).

DISCUSSION

For better clarity and understanding, the discussion was addressed in subdivisions, that is, by disease anxiety and subtopics.

Exercise Versus Intervention

Oeland and colleagues [13] developed a research with 48 patients with symptoms of anxiety and depression, with 30 minutes of aerobic exercise at 65-75% HR reserve and 5 strength exercises for upper and lower limbs with 3x (8-10) repetitions and intensity of 10RM. With the objective to investigate whether they were able to achieve a level of physical activity according to Public Health Recommendations, increase in physical fitness and improvement in quality of life (QoL). All participants maintained their treatments and therapies with their psychiatrists. The sample

was divided into two groups, experimental group n=27 and n=21 control group. The intervention lasted 20 weeks and 12 weeks monitoring. Concluded that the experimental group improved the level of activity in 120min/week and 0.48 mlO2/min VO2max at 20 weeks, and 32 weeks the level of activity decreases in 115min/week. While the control group decreased the level of physical activity for 60 min/week up to 32 weeks. The QoL increased for both groups up to 32 weeks, with no significant difference between groups. The HAM-D scores and Hamilton Rating Scale for Anxiety HAM-A was significantly decreased in both groups by improving mental health with no difference between them. The same way the muscle strength of upper and lower limbs increased at 32

Table 1. Papers that investigated the effets acute or chronic of the exercise in patients with anxiety.

Author Year	Nº Patient	Mean of Age	Training	Medication	Nº of Weeks	Duration of Session or nº Exercises	Days/Weeks	Intensity Controlled	Supervised	Criteria of Diagnostic	Instruments	Level of anxiety	Randomized	Outcomes
Wedekind *et al.*, [15]	GEA=41 GRE=34	32	Aerobic and relaxation	paroxetine	10	45 minutes	4	Yes Moderate	Yes	DSM-IV ICD-10	CGI PAS	Moderate to Severe	Yes	There was significant improvement in the scores of the ICG, to exercise + (paroxetine), compared to placebo + relaxation.
Oeland *et al.*, [13]	GE=27 GC=21	GE=36 GC=40	Aerobic 30min strength 3x (8-10reps.) 10RM	Yes	32	90 minutes	2	Yes, 65 to 75% HR reserve	Yes	ICD-10	HAM-D HAM-A	Mild to moderate	Yes	The experimental group improved the level of activity and VO_2max 120min/week 0.48 mlO_2/min at 20 weeks
Meron *et al.*, [19]	GEA=38 GC=36	GEA=38 GC=39	Aerobic/ Aerobic and Education	No	8 to 10	30 to150 min/week	5	Yes Moderate to intense	Yes	DSM-IV	DASS-21	Mild to moderate	Yes	Significant reduction of the depressive symptoms (DASS) symptoms, for volunteers with social phobia group (EX + CGBT)
Lambert *et al.*, [16]	GLS=57 GG=60	GLS=40 GG=38	Aerobic	Yes	16	30 to 60 minutes	3	---	Yes	DSM-IV	BAI BDI FQ	Moderate to Severe	Yes	There was a significant reduction in anxiety in the exercise group + occupational therapy and changes in lifestyle for ten months compared to GC, and had fewer panic attack at 20 weeks in a significant way.
Brooks *et al.*, [14]	GEA=16 GA=15 GP=15	GE=31 GA=33 GP=34	Aerobic	Clomipramine	10	---	3 to 4	No	Yes	DSM-III-R HARS	ICI BAI BDI CGI	Moderate to Severe	Yes	The exercise was more effective than placebo and less than an antidepressant effective in reducing the symptoms.
Sexton *et al.*, [17]	GEA=28 GC=24	GEA=36 GC=39	Aerobic	No	8	30 minutes	3 to 4	Yes, 70% MHR	Yes	DSM-III	SC-90R STAI BPRS GAS	Moderate to Severe	Yes	Reduction of symptoms in both groups without significant difference, but a greater reduction in running.
Martinsen *et al.*, [20]	GEA=36 GC=47	GEA=39 GC=38	Aerobic Non-aerobic	Yes	8	60 minutes	3	70% $VO_2máx$	Yes	DSM-III-R	CRS PARS ACS	Moderate to Severe	Yes	Significant improvement compared to baseline in both groups, but no difference between them.

Author Year	Nº Patient	Mean of Age	Training	Medication	Nº of Weeks	Duration of Session or nº Exercises	Days/ Weeks	Intensity Controlled	Supervised	Criteria of Diagnostic	Instruments	Level of anxiety	Randomized	Outcomes
Herring *et al.*, [21]	GER=10 GEA=10 GC=10	GEA=20 GR=25 GC=24	Aerobic and strength	Yes	6	46 minutes (strength) 2x16 minutes (aerobic)	2	Yes, 55 to 65% 1RM	Yes	DSM-IV ADIS-IV	NNT BDI	Moderate to Severe	Yes	Remission of 60, 40 and 30% for groups (TRE), (AET) and (GC) respectively. Reduction of concern for (TRE), (EWA) compared to control.
Jazaieri *et al.*, [22]	GEA=25 G (mbsr)=31 GC=29	GEA=32 GE=32 GC=32	Aerobic MBRS	Yes	8	30	2	Yes, moderate	No	DSM-IV ADIS-IV	BDI-II	Moderate to Severe	Yes	Reduction of symptoms (social phobia and depression) and improved well-being for MBSR and AE compared with SAD treated group, but no difference.
Hovland *et al.*, [18]	GE=17 GC=19	GE=38 GC=37	Aerobic and strength	Yes	12	90 minutes	3	60 to 80% MHR	Yes	DSM-IV SCID-I	BDI-II BAI	Moderate to Severe	Yes	There was a significant effect of time and interaction on behalf of CBT group compared to exercise.

GMBSR = Group of Mindfulness-Based Stress Reduction –GEA= Group of Exercise Aerobic - GE = Group Experimental – GA = Group Antidepressant - GC = Group Control – GP = Group Placebo – GER= Group Exercise Resisted – GRE = Group Relaxation - GLS = Group Lifestyle - DSM-IV = Manual Diagnostic e Statistic de Mental Disorders - BAI = Beck Anxiety Inventory – BDI = Beck Depression Inventory - HARS = Hamilton Anxiety Rating Scale score - DASS-21 Depression Anxiety Stress Scale - GED = Group of Exercise and education – PSL = Panic Symptom List = VAAS = Visual Analogue Anxiety Scale - CGI = Clinical Global Impression – PAS = Panic and Agoraphobia Scale – ICD-10 = International Classification for Diseases Tenth Revision - SC-90R - Symptom Checklist 90R – STAI = State-Trait Anxiety Inventory - BPRS = Brief Psychiatric Rating Scale – GAS = Global Assessment Scale - FQ = Fear Questionnaire - CRS = Comprehensive psycho-pathological Rating Scale – PARS = Phobic Avoidance Rating Scale – ACS = Agoraphobic Cognitions Scale - ADIS-IV = Anxiety Disorders Interview Schedule.

weeks, with no significant difference between groups. Patients with anxiety Disorder and/or depression in this study, with the exercise program carried out in consonance with the public health recommendations, had a higher level of physical activity and maximum oxygen uptake.

Exercise Versus Antidepressants Versus Placebo

Brooks and colleagues [14] developed a research of 46 patients with panic disorder with or without agoraphobia, the purpose of this study the therapeutic effect of the exercise was to compare patients with panic disorder to treatment with drugs of proven efficacy and placebo. This study took place at 10 weeks of treatment with aerobic exercise and antidepressant (clomipramine 112.5 mg/day), the groups were randomly divided into: aerobic exercise group, n=16, n=15 clomipramine group and placebo group n=15. Aerobic exercise is: walking four miles in the first week, do the same route in the second week, but with racing shots 2-4 minutes increase the running time in the next 4 weeks and run all the way over the past 4 weeks. The results show that the clomipramine group had better effect than placebo in reducing the symptoms of anxiety using (BAI), Beck Anxiety Inventory, (FQ) Fear Questionnaire and depression (BDI) and (MAS) Montgomery-Åsberg scale but also in scores of CGI, and when the drug Clomipramine was compared to the exercise, had significant results in scores of (FQ and CGI). When compared with placebo, the exercise was more effective in all ranges except the scale version of panic and agoraphobia evaluated by the patient. Possible nonspecific effects, such as increased social interaction may have contributed to the beneficial effect of exercise, for the first month the effect of exercise was not different from placebo, there was also no difference in the self-rating and rating made by the observer. The results suggest that regular

aerobic exercise alone compared to placebo is associated with significant clinical improvement in patients suffering from panic disorder but is less effective than treatment with clomipramine.

Exercise Plus Antidepressants Versus Relaxation Plus Antidepressants Versus Exercise Versus Placebo Plus Relaxation Plus Placebo

Wedekind and colleagues [15] conducted a study in 75 subjects with panic disorders, this study was done at 10 weeks, the sample was divided into two groups: group exercise + antidepressant medication and relaxation +

Table 2. Risk of bias of the papers that investigated the acute and chronic effects of exercise in patients with anxiety.

Study	EC	CG	RD	RS	IR	RDM
Wedekind *et al.*, [15]	Yes	Yes	Yes	No	Yes	Yes
Oeland *et al.*, [13]	Yes	Yes	Yes	No	Yes	No
Meron *et al.*, [19]	Yes	Yes	Yes	No	Yes	Yes
Lambert *et al.*, [16]	Yes	Yes	Yes	No	Yes	Yes
Brooks *et al.*, [14]	Yes	Yes	Yes	No	Yes	Yes
Sexton *et al.*, [17]	Yes	Yes	Yes	No	Yes	Yes
Martinsen *et al.*, [20]	Yes	No	Yes	Yes	Yes	Yes
Herring *et al.*, [21]	Yes	Yes	Yes	Yes	Yes	Yes
Jazaieri *et al.*, [22]	Yes	Yes	Yes	Yes	Yes	Yes
Hovland *et al.*, [18]	Yes	Yes	Yes	Yes	Yes	Yes

EC, Eligibility Criteria; CG, Control Group; RD, Random Distribution; RS, Results from the Minimum of 85% of the Sample; IR, Intergroup Results; RDM, Result Deviation of the Measure.

placebo group. With the objective to examine the effect of combined exercise more antidepressant medication (paroxetine 40mg/day) versus placebo pill plus relaxation for patients with panic disorder with or without agoraphobia. Aerobic exercise was done four times a week for 45 minutes. Outcome was assessed using the Clinical Global Impression (CGI) scale in 10 weeks. There was significant improvement in CGI scores for the exercise group most antidepressant (paroxetine). This study also compared, exercise plus placebo pill against more relaxing more placebo pill using the same scale (Clinical Global Impression Scale). There was however no significant improvement in (CGI) in the exercise group over placebo pill. Exercise cannot replace conventional treatments, such as SSRIs or cognitive behavioral therapy, though, can still be recommended as an additional treatment modality.

Exercise Plus Occupational Therapy Plus Life Style Changes Versus Standard General Practitioner (GP) Care

Lambert and colleagues [16] performed a research in 170 patients in adulthood with anxiety disorders, specifically panic disorders with or without agoraphobia, this study was performed at 16 weeks and 10 months follow-up, divided into two groups: Group 1: occupational therapy + exercise + life style changes; Group 2: Standard general practitioner care (GP). We used the DSM-IV, and psychological tests for the following instruments: Beck Anxiety Inventory, Beck Depression Inventory II and Fear Questionnaire. Altogether 10 intervention sessions were made during a period of 16 weeks (3 sessions of 1h at weekly intervals, 3 half-hour sessions at weekly intervals, 3 half-hour sessions at fortnightly intervals and 1 session of 1hr monthly). The intervention was done in four stages: a) review of lifestyle using self-report, b) Education, c) specific changes in lifestyle and d) monitoring and review in accordance with the lifestyle. The

data showed that significant reduction of anxiety disorders in the exercise group + occupational therapy and changes in lifestyle for ten months compared to the GP group, and had fewer panic attack at 20 weeks significantly, while no significant monitoring phase when compared to the GP group. Changes in life style combined with occupational therapy and exercise seem to provide a clinically effective intervention with significant improvements compared to the treatment of anxiety GP care at the end of treatment.

Moderate/High Intensity Exercise Versus Low Intensity Exercise

Sexton and colleagues [17] conducted a study with 53 volunteers. In this study, the volunteers were divided into two groups, comparing the group light exercise (walking) from heavy exercise or very intense (running) in patients diagnosed with anxiety group. The group exercised for 30 minutes 3-4 weekly for 8 weeks days, the group running with an intensity of 70% of MHR and the walking group did with a comfortable speed. Noted, most non-significant reduction in anxiety symptoms in the running group compared with the walking group, used for the State-Trait Anxiety Inventory (Trait scale) and the State-Trait Anxiety Inventory (State scale). The same way, there was no significant difference between the results of these two groups in the Brief Psychiatric Rating Scale (BPRS). Instead, the results of the Global Assessment Scale (GAS) Results not significantly favored the walk. The authors concluded that therapeutic exercise should be mild, 30 minutes several times a week and regularly, this proved to be effective for the benefit and minimize treatment abandonment of symptomatic neurotic patients, serving as an important complement in the treatment of acute depressive symptoms, chronic anxiety and general neurotic symptoms.

Exercise Versus CBT

Hovland and colleagues [18] performed this recent research, where he recruited 36 patients aged 18-50 years suffering from panic disorder (PD). The objective was to compare exercise with cognitive behavioral therapy (CBT) as a treatment for PD, and evaluate long-term in a controlled manner the significant effects. Patients were divided into two groups: the exercise group (n=17) who performed on the first day of the week: 60 minutes of walking or running 60 to 80% (MHR) by at least 40 minutes, on the second day: circuit training sequences 2-3 of 9 exercises with 15 seconds of each other and 2 minutes between sequence and on the third day consisted of sports and games competition for 60 minutes, but due to the warm-up and calm, all sessions were around 90 minutes. The second group was CBT (n = 19), who performed one session per week. Both treatments were observed for 12 weeks and evaluated twice before the beginning of treatment, post-treatment and at 6 and 12 months. Questionnaires used the following: Mobility Inventory (MI), the Agoraphobia Cognitions Questionnaire (ACQ) and the Body Sensations Questionnaire (BSQ) and diagnostic criteria of PD were used (DSM-IV-TR and SCIDI). Participants who were taking psychotropic medication did it two weeks before, during and two weeks after treatment stabilized and controlled manner. In the present study it was unclear whether the individuals had reduced levels of anxiety due to the level of fitness or 12 weeks of follow-up, though possibly the mechanisms responsible for the benefits were related to: social support, standardization and feedback from colleagues. The data showed a significant effect of time and interaction in favor of CBT group. This was more effective than group exercise in the treatment of panic disorder, both immediately as well as after treatment at follow-up.

Exercise Plus CBT Versus Health Educational Talks Plus CBT

Meron and colleagues [19] completed a study that consisted in the treatment of generalized anxiety disorder, social phobia and panic disorder, comprised the sample of this study, 76 volunteers were divided into two groups: (GCBT + EX) group cognitive therapy more behavioral aerobic exercise and n = 38 (GCBT + ED) group cognitive behavioral therapy plus educational sessions n = 36. Used self-report depression, anxiety, and stress scale (DASS-21). Aerobic exercise consisted of sessions of moderate intensity with 30 minutes of fast walking, where the goal was to attain five or more sessions per week, or at least 150min. The data showed a non-significant reduction in anxiety symptoms after treatment for the group (GCBT + EX) compared to group (GCBT + DE) and there was significant reduction of depressive symptoms for Depression and Anxiety Stress Scale (DASS) when the benefits of exercise combined with cognitive behavioral therapy for subjects with social phobia, these results may have been influenced by the higher numbered with the evaluators and also by the inclusion of feedback. The potential for exercise interventions to GCBT as additional treatment for anxiety disorder need to be further explored.

Aerobic Versus Non-Aerobic Exercise

Martinsen and colleagues [20] performed a research with 79 subjects with anxiety disorders. The sample was divided into two groups: group 1 aerobic exercise, and group 2 no aerobic exercise, with an average age of 39 and 38 years, respectively, for a period of 8 weeks. The exercise was done three times a week with each session lasting 60 minutes, the aerobic group with fast walking or running, reaching 70% of VO2max. The non-aerobic group did strength exercises, stretching and relaxation of low intensity. Diagnostic criteria used in the DSM-IIIR. This study compared the effects of aerobic and non-aerobic exercise in panic disorder, agoraphobia without panic disorder, social phobia and generalized anxiety disorder. At the end of the study, both groups had achieved significant reductions in scores compared with their respective baseline values; there was a small non-significant difference between aerobic and nonaerobic groups. Used the following instruments: Comprehensive Rating Scale psycho-pathological and Phobic Avoidance Rating Scale. The authors concluded by suggesting that the mechanisms responsible for the improvement in anxiety in the present study appear to be psychological, the distraction of the stimuli that causes anxiety, greater self-efficacy and mastery experiences. Herring and colleagues [21] performed a research on 30 women aged between 18 and 39 years, and generalized anxiety disorders (GAD), the aim of this study was to compare the rate of remission and reduction of symptoms of concern among exercise groups and control. The sample was randomly divided into 3 equal groups: endurance training group (TRE), group exercise training (TAE) and control group (CG). Both groups (TRE) and (TAE) conducted two sessions of 46min per week for a period of six weeks. The endurance exercise was performed as follows: 3 years with 7 sets of 10 repetitions each, 80 seconds recovery, intensity 50- 75% of 1RM. Aerobic exercise was done on the ergometer for 46 minutes with intensity 50-75% of the maximum load cycle, monitoring heart rate (HR) and rate of perceived exertion (RPE). The control group had no activity for six weeks with the exception of tests and evaluations. Assessments based on DSM-IV, to measure the extent of anxiety used the Anxiety Disorders Interview Schedule (ADIS-IV), to assess the symptoms of concern were used Psychiatric Diagnostic Screening Questionnaire (PDSQ) and the Penn State Worry Questionnaire (PSWQ). The data showed that the remission rate was 60, 40 and 30% for groups (TRE), (TAE) and (GC) respectively. There was a moderate reduction in symptoms of concern to both groups of

exercises, mainly from the endurance training group compared to the control group, these results may be related to the effect of exercise on a possible reduction in allostatic or neurotrophic load and neuroprotective effects. The exercise training, including (TRE) is a reliable and low-risk treatment that potentially can reduce the symptoms of concern among patients with GAD and can be an effective adjunct in the short-term treatment. Jazaieri and colleagues [22] completed a 8-weeks study in 56 patients with anxiety disorders, specifically social anxiety disorder (SAD), this sample has given rise to two groups: group mindfulness-based stress reduction (MBSR) and aerobic exercise (AE), with 31 and 25 respectively volunteers group. There is even a group apart 48 healthy volunteers and 29 with (TAS) untreated as control group. The aim of this study was to examine the effects of MBSR against EA on clinical symptoms and well-being in adults with SAD. The MBSR group performed eight weekly classes; group meeting for 2.5 hours a meditation retreat (Hatha Yoga) 1 day and daily practice at home. The aerobic group performed two weekly sessions of aerobic exercise with moderate intensity. Participants were assessed at baseline, post-intervention and three months follow-up. Used DSM-IV to measure generalized anxiety disorder (GAD) used the Anxiety Disorders Interview Schedule (ADIS-IV). The data of both MBSR and EA resulted in reductions in clinical symptoms (social phobia and depression) and improves the welfare of both post-intervention and follow-up of 3 months compared to the untreated group TAS. There were no statistically significant differences between the two interventions. Thus, the MBSR and EA needing further investigation as alternative treatments for patients with social anxiety disorder.

Methodological Differences

Among the selected studies examining the effects of exercise alone, Assistant to antidepressant drug or to any other alternative therapy on symptoms of anxiety, we found a range of different outcomes. The factors that may be related to this fact are numerous, such as: severity of symptoms of anxiety, duration of intervention, volume and intensity of exercise and even the fact that the exercise is aerobic or strength. Studies that had their focus on samples with anxiety disorders [13-22] also showed mixed results. Of these, three studies [20-22] analyzed the efficacy of aerobic exercise compared to non-aerobic exercise in reducing anxiety disorders, the first study [20] showed a significant reduction of anxiety disorders for both groups, aerobic and non-aerobic compared the baseline, but with no difference between the groups, with the following exercise protocol: (3x week, 60min, for 8 weeks) aerobic 70% of VO2max (high intensity) and strength (low intensity). The second study [21] used the aerobic exercise (TAE), strength (TRE) and control (CG), one for each group and assessed the effect of these exercises in remission symptoms in patients with generalized anxiety disorder, finding reduction 60, 40 and 30% respectively for (TRE), (TAE) and (GC), although a protocol for short-term, low-intensity, aerobic with (2x week, 46min, for 6 weeks) and exercise with the same methodology, but with intensity 50-75% 1RM, 3 exercises with 7x10 repetitions, were effective in remission. The third study [22] didn't show such consistent results, with a slight decline in symptoms, however no significant difference in exercise groups, this finding may be related to methodological differences between studies because the last used mindfulness-based stress reduction (MBSR) and aerobic exercise group only 2x a week with moderate intensity for 8 weeks.

Neurobiological Mechanisms

The neurobiological effects of exercise appear to influence several neural mechanisms that are related to anxiety disorders [23, 24]. As well as the effect of exercise is compared to the cognitive behavioral therapy or drugs in anxiety disorders [25, 26]. Though, these monoamine levels may be increased with regular and systematic practice of physical exercise. Studies have shown that significant levels of noradrenaline and 5TH, as well as the expression of 5HIAA and 5-HT2C receptors in the limbic system have been reported following exercise on a treadmill of chronic form [27-32]. Another important mechanism that suffers major adaptations is the hypothalamic-pituitary-adrenal system (HPA) subjected to chronic stress has great hyperactivity and elevated levels of glucocorticoids [33, 34], which are harmful to the body. So in this sense, one of the main effects of endurance training is to alter the tissue sensitivity to glucocorticoids [35], another effect of exercise is the activation of the sympathetic nervous system that stimulate the secretion of glucocorticoids [36- 39]. Studies have shown that physically active people have different cortisol responses after acute exercise are attenuated and dissipate more quickly than less active individuals [40-42]. Therefore, exercise can reduce symptoms of anxiety due to their influence on the HPA system and glucocorticoid attenuated response to stressful stimuli. Factor that influences the HPA system is the peptide hormone atrial natriuretic peptide (ANP), which has been observed to inhibit the HPA [43-45] system. The physical activity also increases the plasma concentrations of ANP [46] and anxiolytic effects of exercise correlate with increased plasma concentrations of ANP [47]. Though, one of the mechanisms observed with CBT, tailored to the needs of each patient, is the power to produce volumetric changes in the amygdala, in the case of chronic anxiety [48]. Human studies have shown that a deficiency in the availability of BDNF is associated with vulnerability to depression [49] and this deficiency is reduced after 30 minutes of exercise in patients with panic disorder but not in healthy controls [50] Another mechanism is influenced by exercise Increased the brain growth factor such as brainderived neurotrophic factor (BDNF) expression is related to the effects of exercise on brain plasticity, cognitive functioning and health [51, 52].

CONCLUSION

In this systematic review on the anxiolytic effect of exercise on symptoms of anxiety, we filter and use 10 randomized clinical trials, adding a study sample of 644 subjects. The data presented in this systematic review indicate that 91% of studies that investigated the anxiolytic effect of exercise on anxiety symptoms showed significant results, while 9% of the studies, although not reduce symptoms, improved in general some physiological aspects, such as increased oxygen uptake and physical activity level. The randomized clinical trials reviewed here, could well attend to tighter control of prescription and monitoring of exercise and can thus benefit from better results on the anxiolytic effects of exercise. Regarding the methodology used in exercise protocols, we found that outcomes vary because of different experimental approaches. Volume, intensity and day per weeks, thus making it impossible to weave some feedback from practical application of this analysis: where aerobic exercise, strength, stretching and relaxation, ranging in were used. However, it was observed that aerobic exercise only or adjunctive to other alternative therapies, was effective in reducing symptoms of anxiety, but it is still unknown the best dose-response exercise, lacking other studies.

LIST OF ABBREVIATIONS

5HIAA = 5-Hydroxyindoleacetic Acid

ACQ = Agoraphobia Cognitions Questionnaire

ADIS-IV = Anxiety Disorders Interview Schedule

AE = Aerobic Exercise

BAI = Beck Anxiety Inventory

BDI = Beck depression Inventory

BDNF = Brain-Derived Neurotrophic Factor

BPRS = Brief Psychiatric Rating Scale

BSQ = Body Sensations Questionnaire

CBT = Cognitive Behavioral Therapy

CG = Control Group

CGI = Clinical Global Impression

DASS = Depression and Anxiety Stress Scale

DSM-IV = Diagnostic and Statistical Manual

FQ = Fear Questionnaire

GAD = Generalized Anxiety Disorders

GAS = Global Assessment Scale

GP = General Practitioner Care

HAM-A = Hamilton Rating Scale for Anxiety

HAM-D = Hamilton Rating Scale for Depression

HPA = Hypothalamic-Pituitary-Adrenal

HR = Heart Rate

MAS = Montgomery-Åsberg Scale

MBSR = Mindfulness-Based Stress Reduction

MHR = Maximal Heart Rate

MI = Mobility Inventory

mlO2/min = Mililitro de oxigênio por minute

PD = Panic Disorder

PDSQ = Psychiatric Diagnostic Screening Questionnaire

PSWQ = Penn State Worry Questionnaire

Qol = Quality of life

RM = Repetition Maximal

RPE = Rate of Perceived Exertion

SAD = Social Anxiety Disorder

SSRIs = Selective serotonin reuptake inhibitor

TAE = Aerobic Exercise Training

TRE = Endurance Training

VO2max = Volume de oxigênio máximo

REFERENCES

[1] Coutinho FC, Dias GP, do Nascimento Bevilaqua MC, Gardino PF, Pimentel Range B, Nardi AE. Current concept of anxiety: implications from Darwin to the DSM-V for the diagnosis of generalized anxiety disorder. Expert Rev Neurother 2010; 10: 1307-320.

[2] Tallman JF, Paul SM, Skolnick P, Gallager DW. Receptors for the age of anxiety: pharmacology of the benzodiazepines. Science 1980; 207: 274-81.

[3] Gelder M, Harrison P, Cowen P. Shorter oxford text book of psychiatry. 5th edn. New York: Oxford University Press, 2006; pp. 175-202.

[4] Fountoulakis KN, Vieta E, Sanchez-Moreno J, et al. Treatment guidelines for bipolar disorder: a critical review. J Affect Disord 2005; 86(1): 1-10.

[5] Black et al., 2006 (please provide complete reference including complete list of authors' names, article title, journal name and volume number). [6] Corona et al., 2009 (please provide complete reference including complete list of authors' names, article title, journal name and volume number).

[7] Petruzzello SJ, Landers DM, Hatfield BD, et al. A meta-analysis on the anxiety-reducing effects of acute and chronic exercise. Sports Med 1991; 11(3): 143-82.

[8] Altchiler L, Motta R. Effects of aerobic and nonaerobic exercise on anxiety, absenteeism, and job satisfaction. J Clin Psychol 1994; 50(6): 829-40.

[9] Salmon P. Effects of physical exercise on anxiety, depression, and sensitivity to stress: a unifying theory. Clin Psychol Rev 2001; 21(1): 33-61.

[10] De Araújo SRC, De Mello MT, Leite JR. Transtornos de ansiedade e exercício físico Anxiety disorders and physical exercise. Rev Bras Psiquiatr 2007; 29(2): 164-71.

[11] Jayakody K, Gunadasa S, Hosker C. Exercise for anxiety disorders: systematic review. Br J Sports Med 2013; 48(3): 187-96.

[12] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009; 151(4): 264-9.

[13] Oeland AM, Laessoe U, Olesen AV, et al. Impact of exercise on patients with depression and anxiety. Nordic J Psychiatry 2010; 64(3): 210-7.

[14] Broocks A, Bandelow B, Pekrun G, et al. Comparison of aerobic exercise, clomipramine, and placebo in the treatment of panic disorder. Am J Psychiatry 1998; 155(5): 603-9.

[15] Wedekind D, Broocks A, Weiss N, et al. A randomized, controlled trial of aerobic exercise in combination with paroxetine in the treatment of panic disorder. World J Biol Psychiatry 2010; 11(7): 904-13.

[16] Lambert RA, Harvey I, Poland F. A pragmatic unblinded randomised controlled trial comparing an occupational therapy-led lifestyle approach and routine GP care for panic disorder treatment in primary care. J Affect Disord 2007; 99(1): 63-71.

[17] Sexton H, Mære Å, Dahl NH. Exercise intensity and reduction in neurotic symptoms. Acta Psychiatr Scand 1989; 80(3): 231-5. [18] Hovland A, Nordhus IH, Sjøbø T, et al. Comparing physical exercise in groups to group cognitive behaviour therapy for the treatment of panic disorder in a randomized controlled trial. Behav Cogn Psychotherapy 2013; 41(04): 408-32.

[19] Merom D, Phongsavan P, Wagner R, et al. Promoting walking as an adjunct intervention to group cognitive behavioral therapy for anxiety disorders—a pilot group randomized trial. J Anxiety Disord 2008; 22(6): 959-68.

[20] Martinsen E, Hoffart A, Solberg ØY. Aerobic and nonaerobic forms of exercise in the treatment of anxiety disorders. Stress Med 1989; 5(2): 115-20.

[21] Herring MP, Jacob ML, Suveg C, et al. Feasibility of exercise training for the short-term treatment of generalized anxiety disorder: a randomized controlled trial. Psychotherapy Psychosom 2001; 81(1): 21-8.

[22] Jazaieri H, Goldin PR, Werner K, et al. A randomized trial of MBSR versus aerobic exercise for social anxiety disorder. J Clin Psychol 2012; 68(7): 715-31.

[23] Fuss J, Ben Abdallah NMB, Vogt MA, et al. Voluntary exercise induces anxiety-like behavior in adult C57BL/6J mice correlating with hippocampal neurogenesis. Hippocampus 2010; 20(3): 364- 76.

[24] Cassilhas RC, Antunes HKM, Tufik S, et al. Mood, anxiety, and serum IGF-1 in elderly men given 24 weeks of high resistance exercise. Percept Mot Skills 2010; 110(1): 265-76.

[25] Wipfli BM, Rethorst CD, Landers DM. The anxiolytic effects of exercise: A meta-analysis of randomized trials and dose-response analysis. J Sport Exerc Psychol 2008; 30: 392-410.

[26] Rossy LA, Buckelew SP, Dorr N, et al. A meta-analysis of fibromyalgia treatment interventions. Ann Behav Med 1999; 21(2): 180-91.

[27] Gordon R, Spector S, Sjoerdsma A, et al. Increased synthesis of norepinephrine and epinephrine in the intact rat during exercise and exposure to cold. J Pharmacol Exp Ther 1966; 153(3): 440-7.

[28] Barchas JD, Freedman DX. Brain Amines: Response to Physiological Stress. Biochem Pharmacol 1963; 12: 1232-5.

[29] Chaouloff F, Elghozi JL, Guezennec Y, et al. Effects of conditioned running on plasma, liver and brain tryptophan and on brain 5-hydroxytryptamine metabolism of the rat. Br J Pharmacol 1985; 86(1): 33-41.

[30] Acworth I, Nicholass J, Morgan B, et al. Effect of sustained exercise on concentrations of plasma aromatic and branched-chain amino acids and brain amines. Biochem Biophys Res Commun 1986; 137(1): 149-53.

[31] Greenwood BN, Strong PV, Loughridge AB, et al. 5-HT2C receptors in the basolateral amygdala and dorsal striatum are a novel target for the anxiolytic and antidepressant effects of exercise. PLoS One 2012; 7(9): e46118.

[32] Maniam J, Morris MJ. Voluntary exercise and palatable high-fat diet both improve behavioural profile and stress responses in male rats exposed to early life stress: role of hippocampus. Psychoneuroendocrinology 2010; 35(10): 1553-64.

[33] Lupien SJ, Buss C, Schramek TE, et al. Hormetic influence of glucocorticoids on human memory. Nonlinearity Biol Toxicol Med 2005; 3(1): 23-56.

[34] Pruessner JC, Hellhammer DH, Kirschbaum C. Burnout, perceived stress, and cortisol responses to awakening. Psychosom Med 1999; 61(2): 197-204.

[35] Duclos M, Gouarne C, Bonnemaison D. Acute and chronic effects of exercise on tissue sensitivity to glucocorticoids. J Appl Physiol 2003; 94(3): 869-75.

[36] Droste SK, Chandramohan Y, Hill LE, et al. Voluntary exercise impacts on the rat hypothalamic-pituitary-adrenocortical axis mainly at the adrenal level. Neuroendocrinology 2007; 86(1): 26- 37.

[37] Droste SK, Gesing A, Ulbricht S, et al. Effects of long-term voluntary exercise on the mouse hypothalamic-pituitaryadrenocortical axis. Endocrinology 2003; 144(7): 3012-23.

[38] Budde H, Pietrassyk-Kendziorra S, Bohm S, et al. Hormonal responses to physical and cognitive stress in a school setting. Neurosci Lett 2010; 474(3): 131-134.

[39] Budde H, Voelcker-Rehage C, Pietrassyk-Kendziorra S, et al. Steroid hormones in the saliva of adolescents after different exercise intensities and their influence on working memory in a school setting. Psychoneuroendocrinology 2010; 35(3): 382-391.

[40] Luger A, Deuster PA, Kyle SB, et al. Acute hypothalamicpituitary-adrenal responses to the stress of treadmill exercise. Physiologic adaptations to physical training. N Engl J Med 1987; 316(21): 1309-15.

[41] Rudolph DL, McAuley E. Cortisol and affective responses to exercise. J Sports Sci 1998; 16(2): 121-8.

[42] Mathur DN, Toriola AL, Dada OA. Serum cortisol and testosterone levels in conditioned male distance runners and nonathletes after maximal exercise. J Sports Med Phys Fitness 1986; 26(3): 245-50.

[43] Kellner M, Wiedemann K, Holsboer F. Atrial natriuretic factor inhibits the CRH-stimulated secretion of ACTH and cortisol in man. Life Sci 1992; 50(24): 1835-42.

[44] Kellner M, Herzog L, Holsboer F, et al. Circadian changes in the sensitivity of the corticotropin-releasing hormones-stimulated HPA system after arginine vasopressin and atrial natriuretic hormone in human male controls. Psychoneuroendocrinology 1995; 20(5): 515- 524.

[45] Ströhle A, Kellner M, Holsboer F, et al. Atrial natriuretic hormone decreases endocrine response to a combined dexamethasonecorticotropin-releasing hormone test. Biol Psychiatry 1998; 43(5): 371-5.

[46] Mandroukas K, Zakas A, Aggelopoulou N, et al. Atrial natriuretic factor responses to submaximal and maximal exercise. Br J Sports Med 1995; 29(4): 248-51.

[47] Ströhle A, Feller C, Strasburger C, et al. Anxiety modulation by the heart? Aerobic exercise and atrial natriuretic peptide. Psychoneuroendocrinology 2006; 31(9): 1127-30.

[48] Neves-Pereira M, Mundo E, Muglia P, et al. The brain-derived neurotrophic factor gene confers susceptibility to bipolar disorder: evidence from a family-based association study. Am J Hum Genet 2002; 71(3): 651-5.

[49] Hölzel BK, Carmody J, Evans KC, et al. Stress reduction correlates with structural changes in the amygdala. SCAN 2010; 5(1): 11-17.

[50] Ströhle A, Stoy M, Graetz B, et al. Acute exercise ameliorates reduced brain-derived neurotrophic factor in patients with panic disorder. Psychoneuroendocrinology 2012; 35(3): 364-8.

[51] Cotman CW, Berchtold NC, Christie LA. Exercise builds brain health: key roles of growth factor cascades and inflammation. Trends Neurosci 2007; 30(9): 464-72.

[52] Marais L, Stein DJ, Daniels WM. Exercise increases BDNF levels in the striatum and decreases depressive-like behavior in chronically stressed rats. Metab Brain Dis 2009; 24(4): 587-97.