



TREATMENT FOR GENERALIZED ANXIETY DISORDER THROUGH PHYSICAL EXERCISE: A SYSTEMATIC REVIEW

REVIEW ARTICLE

MOURA, Denésio de Oliveira¹, MOREIRA, Elisângela Claudia de Medeiros², DIAS, Claudio Alberto Gellis de Mattos³, FECURY, Amanda Alves⁴, DENDASCK, Carla Viana⁵, SOUZA, Keulle Oliveira da⁶, PIRES, Yomara Pinheiro⁷, SERUFFO, Marcos César da Rocha⁸, BAHIA, Mirleide Chaar⁹, OLIVEIRA, Euzébio de¹⁰

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ABSTRACT

Introduction: Physical exercise improves various physical abilities, as well as it can promote improvement in the clinical condition of several diseases, including those related to the central nervous system. In this sense, the objective of this work was to produce a systematic review of the literature to investigate whether exercise is capable of promoting improvement in the clinical condition in human adults diagnosed with generalized anxiety disorder, whether there is a specific physical exercise, as well as whether the intensity of it is related to the improvement in the disease.

Methods: Randomized clinical trials published up to May 2019 were searched in online databases (PubMed, Scopus, Web of Science, Cochrane Library, LILACS, OpenGrey and Google Scholar) after developing a PICO statement focused on comparison between adults who received an intervention with the practice of regular, planned and supervised physical exercises, compared with sedentary participants and after verifying their effects in the context of generalized anxiety disorder. The search and data extraction were performed following the guidelines of the PRISMA manuscript writing guide. Quality assessment and risk of bias were analyzed following the Cochrane – RoB 2.0 protocol.



Results: A total of 4694 reference articles were retrieved/searched, while only six were considered eligible for the present review. Most articles showed a reduction in generalized anxiety disorder from an intervention with physical, aerobic and anaerobic exercises of moderate intensity. However, in the risk of bias analysis, all articles showed some concerns regarding the reported evidence.

Conclusion: Physical exercise is a potential tool for reducing generalized anxiety disorder, and moderate exercise intensity is directly related to an improvement in the clinical condition of the disease, regardless of the type: aerobic or anaerobic. However, it is important that further research seek to investigate the physiological and neuroendocrine mechanisms related to such improvement.

Keywords: Physical exercise, Anxiety, Systematic review.

INTRODUCTION

Physical Exercise (PE) is considered a subcategory of physical activity, which is usually used to improve the individual's physical abilities, such as: strength, flexibility, muscular endurance and aerobic capacity (GARBER *et al.*, 2011). PE is able to promote a series of physiological changes, which can positively impact human health, and these benefits depend on its correct planning and application, in which it is necessary to take into account the various training variables such as the specificity of exercise, which promotes physiological responses according to each type of activity. For example, aerobic training is reported as important implements to improve, primarily, the cardiovascular capabilities of individuals, as well as strength training improves neuromuscular capabilities (AMERICAN COLLEGE OF SPORTS MEDICINE, 2009).

However, in recent decades, the practice of PE has gone beyond the improvement/development of physical abilities, as it has been shown that physical exercise can promote physiological changes capable of protecting individuals from damage to health, as well as minimizing damage to who is affected by a certain disease or physiological limitation (HAJIZADEH MALEKI *et al.*, 2018). Based on these findings, PE has become a common practice for the prevention and treatment of a series of diseases, including those that compromise the Central



Nervous System (CNS), including Parkinson's disease, which can be minimized through practice of strength training (LEAL *et al.*, 2019) and for Alzheimer's, where aerobic exercise is more effective as one of the treatment strategies (CHEN *et al.*, 2016). In addition to these, other diseases that come from an imbalance in the CNS can be prevented with the practice of PE, among which depression and Generalized Anxiety Disorder (GAD) can be highlighted, diseases that are directly related to important hormonal changes that occur in the CNS (HARVEY *et al.*, 2018).

Anxiety (within moderate levels - accepted by the Brazilian Society of Psychiatry) is a natural physiological alteration of everyday life, and therefore is even considered fundamental to human survival. However, when unbalanced, it becomes a serious neuroendocrine disorder and consequently generates physiological dysfunctions, which can be highly harmful for the person affected by this disorder, since in most cases it manifests itself through the main classic symptoms, such as: excessive sweating, persistent nervousness, tremors, muscle tension, heart palpitations, epigastric discomfort, even literally paralyzing the person with this disorder. Although anxiety is a normal, natural condition and in certain aspects even necessary for human beings, acting as a form of propulsion for people to have the reactions and attitudes necessary for their own survival, when it rises disproportionately and persistently, can induce GAD, triggering a series of problems for the individual with this disorder. This condition directly interferes in the lives of diagnosed individuals, as well as the people who live with them, affecting daily activities, such as social and other spheres (ICD 10).

GAD is one of the diseases for which non-drug treatment alternatives have been sought, such as the practice of yoga, dance and PE. However, it is not clear whether PE is effective, nor what is the characteristic of the exercise (aerobic or anaerobic), as well as the intensity at which safe results are obtained, since investigations have shown that just walking (MA *et al.*, 2017) and in an intense strength training (80% of a maximum repetition – 1RM) (FOCHT and KOLTYN,



1999), the EF caused improvement for these patients. In this sense, the objective of this work was to produce a systematic review of the literature to investigate whether PE is capable of promoting improvement in adult humans diagnosed with GAD, as well as which models and intensities of exercises are related to the improvement of the clinical condition of this disease.

MATERIAL AND METHODS

RECORD

This systematic review was recorded in the PROSPERO database, created by the University of York, which is responsible for registering and disseminating systematic reviews, and performed according to Moher *et al.* (2009), through the PRISMA guide (Preferred Reporting Requirements for Systematic Review and Meta-Analysis) (Figure 1).

SEARCH STRATEGY AND ELIGIBILITY CRITERIA

The PICO strategy was used in this systematic review. PICO stands for Patient, Exposure, Comparison, and Outcome. These components are essential for the design of all stages of the review. Intervention studies in adult humans (P) were included in which patients underwent PE (I) and absence of PE (C) were part of the same investigation, to observe whether there is an association between the practice of PE and the improvement in the symptomatic condition of GAD (O). Review articles, case reports, descriptive studies, opinion articles, technical articles, guidelines, animal and in vitro studies were discarded.

This review was carried out based on the guiding question: “Can physical exercise be an alternative therapeutic intervention to treat generalized anxiety disorder? ”. Searches were carried out in the following electronic databases: PubMed, Scopus, Web of Science, Lilacs, Cochrane, OpenGrey and Google Scholar. During the



searches, there were no restrictions regarding the date of publication and the language used in the studies. All relevant studies were translated and reviewed. The MeSH terms, keywords and search strategy were adapted according to each database, as represented in (Table 1). The searches were performed between March and July 2019.

After carrying out searches in the databases, a weekly search alert was created to notify new studies that fit the search strategy. All relevant articles were entered into a bibliographic reference manager (EndNote®, version X7, Thomson Reuters, Philadelphia, USA). All procedures, including searches, study selection, risk of bias assessment and data extraction were performed independently by two reviewers (DM and MGC) and checked by a third reviewer in case of disagreement (EO).

Duplicate articles were removed through the bibliographic reference manager (EndNote®, version X7, Thomson Reuters, Philadelphia, USA), from automatic exclusion and followed by manual review.

After removing duplicate articles, studies were selected in two moments: first, after reading the title and abstract, and later, after analyzing the full text, according to the previously established eligibility criteria.

DATA EXTRACTION AND QUALITY ASSESSMENT

In the selected articles, data referring to the authors, year of publication, study design, characteristics of the participants (source and sample size), average age, GAD evaluation protocol, type/protocol of the PE applied, were extracted and tabulated, results and statistical analysis (Table 1).

To assess the methodological quality and risk of bias, a “checklist” contained in RoB 2.0 was used, a revised tool to assess the risk of bias in randomized studies (HIGGINS *et al.*, 2016). This “checklist” has domains related to the study and



sample design, characteristics of the control group, quality of measurements and results, and integrity and distorting influences.

For each criterion evaluated in the “checklist”, a “high risk of bias” was attributed to cases of major problems in the study; “some problems”, in case of minor problems and “low risk of bias” for studies that did not present any problems. This tool seeks to assess whether the methods are adequate to produce consistent and valid information, as well as whether the results offered the expected effects (Chart.1).

Chart 1. Data extraction from articles included in the review

Autores	Desenho de estudo	Participantes	Idade	Diagnóstico de transtorno da ansiedade	Exercício e avaliação	Análise estatística	Resultados	Desfecho
DiLorenzo TM et al., 1999	Estudo controlado randomizado	111 - 68% adultos mulheres	Media de idade: 33.5 anos	Inventário de Estado-Traço de Ansiedade e (STAI)	Foi solicitado que os indivíduos se exercitassem em 70-85% da reserva de pico de frequência cardíaca, estimada em teste em bicicleta ergométrica. O protocolo de exercício foi de 12 semanas usando uma bicicleta estacionária, sendo exercício de intensidade variável de 24 minutos (grupo 1) e intensidade fixa de 48 minutos exercícios contínuos (grupo 2), quatro vezes por semana.	Análise multivariada	Para medidas de ansiedade, a interação entre grupo e tempo foi confiável, Wilks' $\Lambda = 0,93$, $F(3, 106) = 2,61$, $P < 0,05$	Os dois protocolos foram eficientes em 12 semanas de programa de exercícios, nos efeitos fisiológicos sem diferença entre eles
Focht and Koltym, 2004	Estudo controlado randomizado	84 51 homens e 33 mulheres	não informado	Inventário de Estado-Traço de Ansiedade e (STAI)	Indivíduos separados aleatoriamente (randomizados) em 50% 1RM, três séries, 12 a 20 repetições por série, intervalo de recuperação de 45 a 75 segundos entre cada série ou 80% de 1RM, três séries de 4 a 8 repetições por série, usando 120 a 150 segundos de intervalo de	ANOVA utilizando pós testes de Tukey.	Um efeito significativo dos ensaios ($F 5, 405 = 16,03$, $P < 0,05$) e ensaios \times interação condição ($F 10, 405 = 4,06$, $P < 0,05$) foram observados para estado de ansiedade. Análises post-hoc indicaram que o estado de ansiedade foi significativamente reduzida 180 min após a condição de	Um ataque agudo de ER a 50% 1RM está associado a uma diminuição no estado de ansiedade que emergiu 180 min após o exercício.

					recuperação.		intensidade de 50% de 1RM, enquanto não foram detectadas alterações significativas para a condição de 80% de 1RM ou controles	
Herring et al., 2011	Estudo controlado randomizado	N=30 Mulheres	18 a 37 anos	Inventário de Estado-Traço de Ansiedade e (STAI)	Sete séries de 10 repetições de exercício resistido de moderadas intensidade (50% e 60% 1-RM) ou realizou duas sessões de 16 min de ciclismo por semana. Média de 122 bpm Exercício percepções subjetivas de esforço - Borg 6e20 (8) e Borg 6e20 (9), consecutivas.	Testes qui-quadrado (χ^2 Cramér's V)	O treinamento de resistência - tamanhos de efeito de seis semanas de Hedges de 0,52 (-0,37, 1,41) e o treinamento aeróbio - Tamanhos de efeito de Hedges 0,54 (-0,36, 1,43) resultaram em melhorias comparáveis em traço de ansiedade.	O treinamento de resistência e o treinamento aeróbio de curto prazo provocam melhorias comparáveis nos sinais e sintomas associados à ansiedade.
Ma et al., 2016	Estudo controlado randomizado	83 adultos	Controle 40.45 anos Experimental 39.76 anos	Inventário de Estado-Traço de Ansiedade e (STAI)	Prática de exercício regular 30 min por dia, 5 dias por semana por um período de 3 meses. Participantes no grupo experimental recebeu tanto o programa de exercícios HB quanto cuidado tradicional.	teste t / análise de variância	os resultados revelaram reduções significativas no estado de ansiedade ($F = 9,35, p = 0,000$) e traço ansiedade ($F = 6,18, p = 0,003$) no grupo experimental em relação ao grupo controle desde o pré-teste até o teste de acompanhamento.	O programa de exercícios feito em casa (home-based - HB) produziu efeitos positivos nos indicadores metabólicos e nos níveis de Adultos taiwaneses com transtornos de ansiedade.
LeBouthillier and Asmundson, 2017	Estudo controlado randomizado	48 homens/mulheres	20 a 40 anos	Entrevista Clínica Estruturada para DSM-5- Versão de Pesquisa. (SCID-5-RV)	Os participantes completaram 40 minutos de exercício aeróbico em uma bicicleta estáacionária (spin cycle) a 60-80% da frequência cardíaca máxima de reserva, ajustada pela idade). O treinamento de resistência envolveu 2-3 séries de 10-12 repetições nas seguintes máquinas: leg press, machine chest press, machine hamstring curl, dumbbell single arm row, machine shoulder press, machine triceps	Testes qui-quadrado (χ^2 Cramér's V)	Para ansiedade, exercício aeróbico foi associado a uma redução em relação à lista de espera 4,75 pontos de pré para pós-intervenção (Cohen's $d = -1,03, IC 95\% [-1,70, -0,38]$); no entanto, não foram observadas mudanças significativas no treinamento de resistência (Cohen's $d = -0,52 IC95\% [-1,29, 0,28]$). Para sensibilidade à ansiedade, os resultados não revelaram alterações em relação à lista de espera ou ao exercício	Tanto o exercício aeróbico quanto o treinamento de resistência parecem ser eficaz na efetivação de melhorias nos sintomas de transtornos relacionados à ansiedade e constructs.



					extension, and machine bicep curl		aeróbico(Cohen é d = -0,23, IC 95% [-0,71, 0,23]); no entanto, o treinamento resistido foi associado com um decréscimo relativo de 13.10 pontos em comparação com a lista de espera (cohen's d = -0.79 (95% IC [-1,34, -0,26])).	
Edwards et al., 2017	Estudo controlado randomizado	N = 110 mean age = 21.4 years	18 a 35 anos – média 21.4	Inventário de Estado-Traço de Ansiedade (STAI)	Participantes foram encorajados a auto-selecionar uma caminhada em ritmo rápido. Especificamente, os participantes foram solicitados a “selecionar um ritmo que andariam se estivessem atrasados para a aula, uma reunião ou para tentar pegar o ônibus”, e para escolher uma velocidade que pudessem manter durante o protocolo. A caminhada foi feita em uma esteira. todas as intervenções duram 10 minutos.	ANOVA e qui-quadrado.	A caminhada (P = 0,75) não mostrou diferença significativa em relação ao grupo controle (P = 0,45 para redução da ansiedade).	Uma breve caminhada reduziu significativamente o estado de ansiedade em jovens adultos.

Source: Data from the survey itself.

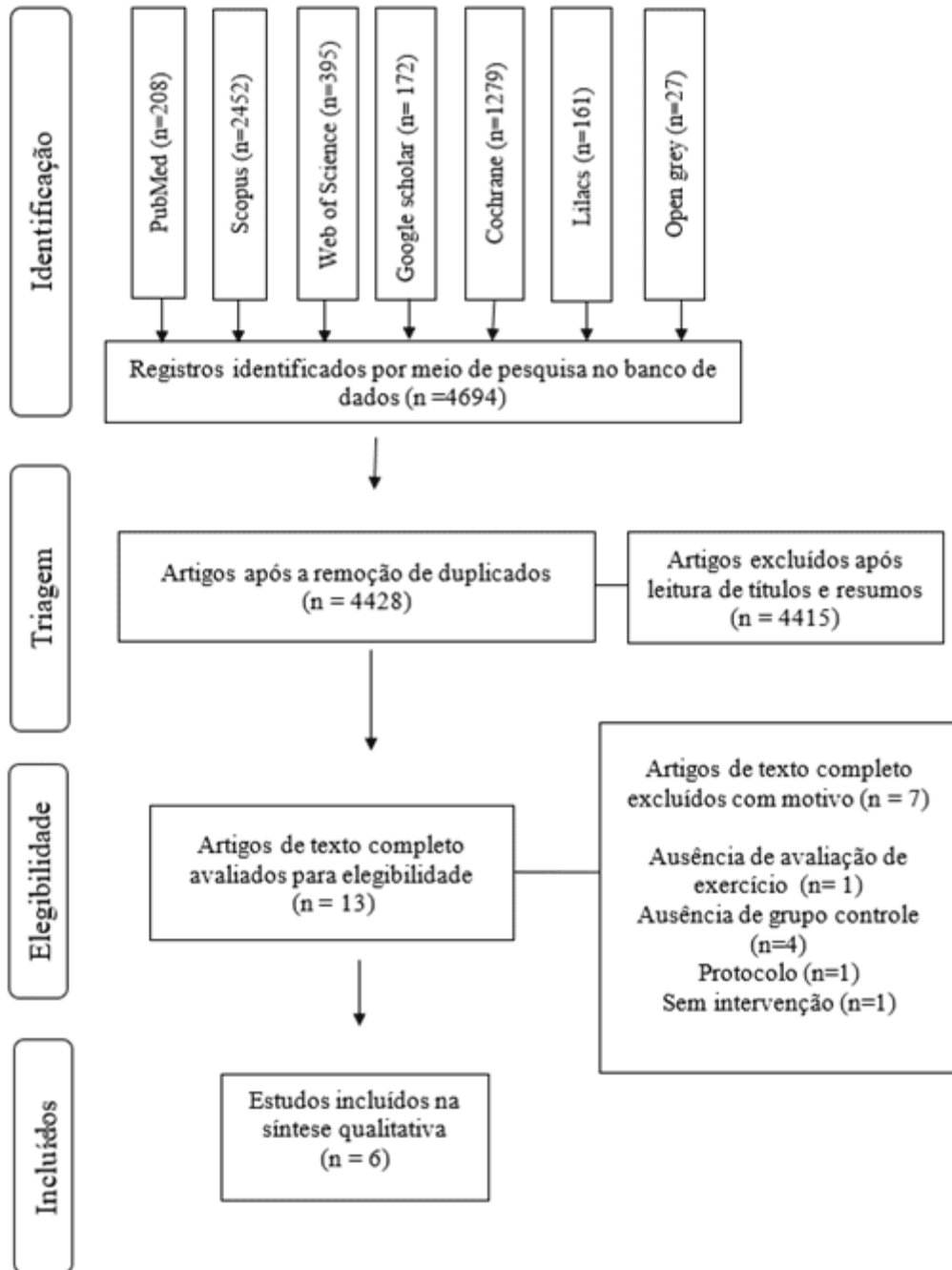


RESULTS

CHARACTERISTICS AND SELECTION OF STUDIES

Among the 4694 references identified in search databases, 266 duplicates were removed. After reading titles and abstracts, 4415 of the 4428 references were excluded based on eligibility criteria. Thus, 13 references were selected for full-text evaluation. Subsequently, one study was excluded due to lack of exercise assessment, four studies were excluded because the authors did not assess participants in the control groups, one reference was excluded because it was a protocol article, and one study was excluded because no intervention was applied to participants. Finally, six articles were eligible for qualitative evaluation (Fig. 1).

Figure 1. Flowchart of database searching according to the PRISMA statement



Source: Author.



INDIVIDUAL STUDY RESULTS

Six Randomized Clinical Trials (RCTs) were included. The effects of PE on GAD were reported in all six selected studies. GAD assessment scales were mostly used by the authors (DILorenzo *et al.*, 1999; FOCHT and KOLTYN, 1999; HERRING *et al.*, 2011; LEBOUTHILLIER, 2017; MA *et al.*, 2017; EDWARDS *et al.*, 2018). The STAI scale (State-Trait Anxiety Inventory) was the choice of all studies to assess the effect of PE on GAD.

Interventions related to the PE with the purpose of minimizing the effects of the GAD varied, in duration: from the immediate evaluation of the tests applied to intervention programs of 6 and 12 weeks, being: the programs of twelve weeks (DILorenzo *et al.*, 1999; MA *et al.*, 2017); six-week programs (HERRING *et al.*, 2011) of immediate intervention (FOCHT and KOLTYN, 1999; LEBOUTHILLIER, 2017; EDWARDS *et al.*, 2018). Physical training applied as an intervention involved aerobic activities (DILorenzo *et al.*, 1999; HERRING *et al.*, 2011; MA *et al.*, 2017) and muscle strength (FOCHT and KOLTYN, 1999; LEBOUTHILLIER, 2017). Associated with the interventions, other physical activities were applied: yoga (MA *et al.*, 2017), Tai-Chi (MA *et al.*, 2017), aerobic dance (MA *et al.*, 2017) and meditation (Edwards *et al.*, 2018). Demographic variables were considered for the analysis of interventions in all studies.

PE was associated with improvements in GAD symptoms, such as: tension anxiety (HERRING *et al.*, 2011), trait anxiety (State-Trait Anxiety (FOCHT and KOLTYN, 1999; MA *et al.*, 2017; EDWARDS *et al.*, 2018), anxiety sensitivity (LEBOUTHILLIER, 2017), anxiety tolerance (LEBOUTHILLIER, 2017) and uncertainty intolerance (LEBOUTHILLIER, 2017). Among the types of PE, both aerobic ones (DILorenzo *et al.*, 1999; HERRING *et al.*, 2011; LEBOUTHILLIER,



2017), and muscle strength (HERRING *et al.*, 2011; LEBOUTHILLIER, 2017) were associated with improvement in GAD.

QUALITATIVE ANALYSIS OF STUDIES

Considering the qualitative analysis using the RoB 2.0 tool (Cochrane) (HIGGINS *et al.*, 2016), the six studies presented the “Some concerns” classification. The biggest problems presented were related to randomization and allocation of groups. This occurrence was due to the lack of description, by the authors, of how the random sequence was generated, only stating that the groups would have been randomized prior to the interventions.

RISK OF BIAS

The risks of bias in the studies are reported in figure 2. None of the studies showed a high risk of bias despite problems related to the sample, such as: allocation, sampling method and randomization of groups. Thus, the overall quality of evidence tends to be reduced due to a non-probabilistic distribution of the characteristics of the groups. All studies were rated as having some concerns regarding the effects of PE in the treatment of GAD.

DISCUSSION

The objective of this study was to look for evidence that would point to the effects of the practice of PE in the treatment of GAD and, based on this, to point out whether this could be a therapeutic strategy for this disease. Randomized studies and systematic reviews of these studies provide the most reliable evidence about the effects of health interventions. Systematic reviews aim to collect and synthesize all studies that meet pre-specified eligibility criteria, using methods that attempt to minimize bias in order to obtain reliable conclusions (HIGGINS *et al.*, 2016).



In this systematic review, it was possible to point out that, among the main therapeutic benefits that PE is able to promote to individuals who present GAD, it is possible to highlight a great improvement in the symptomatology of exacerbated anxiety, especially in the control or reduction of tension resulting from the GAD (HERRING *et al.*, 2011) in the State-Trait Anxiety (which refers to a personal disposition, to respond with exacerbated anxiety to stressful situations and a tendency to perceive a greater number of situations as threatening, even when they are are not) (DILORENZO *et al.*, 1999; FOCHT and KOLTYN, 1999; MA *et al.*, 2017; EDWARDS *et al.*, 2018), improvement in sensitivity to anxiety and greater tolerance to distress (LEBOUTHILLIER, 2017). These results may be related to biological changes (physiological and neuroendocrine) including in the CNS, promoted by the practice of PE (FERNANDES *et al.*, 2018).

Studies have shown that PE, in addition to promoting improvements in general physical abilities such as strength, flexibility, muscular endurance and aerobic endurance, is capable of preventing systemic diseases such as diabetes (REŞAT DABAK *et al.*, 2019), as well as reducing symptoms of diseases that affect the CNS (HARVEY *et al.*, 2018). GAD may be one of those alterations/diseases that are directly related to the breakdown of CNS activity homeostasis, which can be attenuated by the practice of PE, as we saw in our results.

In fact, it has already been shown that PE is capable of promoting positive adaptations in the CNS, which can be triggered by increasing the synthesis and expression of growth factors, such as Brain Derived Neurotrophic Factor (BDNF), a substance essential for the maintenance of cellular activity in this organ (PHILLIPS, 2017). These physiological/neuroendocrine responses arising from the practice of PE, mainly the synthesis of these growth factors, may be the key to the mechanisms that make the brain less susceptible to imbalances capable of leading to diseases such as GAD, as the results of this investigation have shown that PE is able to reduce the clinical condition of this disease, in which the individuals were before the intervention.



The interventions used in the selected articles rely on both primarily aerobic PE and primarily anaerobic exercises (muscle strength exercises). This is an interesting factor for this investigation, since most of the articles that point to PE as a strategy to improve the functioning of the CNS, normally promote interventions with aerobic PE (FERNANDES *et al.*, 2018). In this sense, there would be another common factor in this, for these two models of PE, which would be promoting the improvement in the GAD framework, since both the aerobic exercise (DILorenzo, 1999; LeBouthillier, 2017; Herring, 2011), and the of muscle strength (LeBouthillier, 2017; Herring, 2011) were effective in the treatment of this disease.

However, it should be noted that during some of the PE practices, these were not effective, such as those associated with aerobic exercises, possibly those of low intensity (a short walk for example) (MA, 2016). As well as strength training, characteristically more intense (80% of 1RM), which did not promote improvement in the GAD clinical condition (FOCHT and KOLTYN, 1999), which possibly points to the fact that physical exercises are practiced at an ideal/standard intensity to contribute to the treatment of GAD. Or even that they ensure better results against this disease and, in this case, it is the practice of PE with moderate intensity, because regardless of the PE, this was a common variable to all the works that proved to be efficient in the treatment of this psychic disorder (DILorenzo *et al.*, 1999; FOCHT and KOLTYN, 1999; HERRING *et al.*, 2011; LeBOUTHILLIER, 2017; MA *et al.*, 2017; EDWARDS *et al.*, 2018).

To point out the practice of PE as a treatment strategy for GAD, it is important to quantify the intensity variable. In the articles selected for this systematic review, the exercise intensity was one of the main conditions controlled during the interventions, as well as the quality of the measurement tools, since this is a methodological variable, which requires individualized measurement for the prescription of training, as in addition to making the practice of PE safer, it



improves the results achieved (AMERICAN COLLEGE OF SPORTS MEDICINE, 2009).

Among the tools for assessing intensity, there are VO₂ max tests, which are normally used for prescribing aerobic exercise, as well as the one repetition maximum test (1RM) and the submaximal repetitions test, recommended by the American College of Medicine of the Sport (GARBER *et al.*, 2011). These tests provide greater reliability in the results of the articles, as well as representing a determining factor for our conclusions.

Another point to take into account is that, although other interventions were used and some of the works, of the studies that used more than one intervention strategy (MA *et al.*, 2017; EDWARDS *et al.*, 2018), were extracted only data from the groups that were included in this review (groups: with PE and without PE). Because, in addition to being a methodological requirement for systematic reviews, this enhances the isolation of variables and reduces the risk of bias in the application of PE as a GAD treatment strategy.

Furthermore, in the case of this investigation, it is important to point out that reliable tools were used (one repetition maximum test – 1RM) (AMERICAN COLLEGE OF SPORTS MEDICINE, 2009), such as for GAD diagnosis (STAI - State-Trait Anxiety Inventory, Inventário State-Trait Anxiety), which can bring greater security in the results obtained by the authors, since these protocols are already well established in the literature, as they have been used for decades for GAD analysis (KNIGHT *et al.*, 1983; LEBOUTHILLIER, 2017; EDWARDS *et al.*, 2018).

Therefore, the fact that the assessment of the GAD levels of the participants was carried out using STAI, in more than 80% of the individuals included in the studies that make up this systematic review, corroborates the fact that this is a tool mostly used when the objective is to evaluate the GAD in medical research and,



consequently, allows us to state that the conclusions obtained in the articles included in this work are safe, which can reduce biases in this investigation (JULIAN, 2011; HIGGINS *et al.*, 2016).

The risk of bias in the studies was assessed using the RoB 2.0 tool, which presents a series of requirements that the study must comply with in order to strengthen its findings. The evaluation of studies was performed for each domain shown in Table 1 (HIGGINS *et al.*, 2016). One of the problems we found in all the studies concerned the randomization criteria, which is certainly the main reason why the articles did not reach maximum quality (low risk of bias), since randomization must ensure that the participants in the intervention and comparison groups are similar with regard to known and unknown prognostic factors, so differences in results can be attributed to the causal effect of the intervention (HIGGINS *et al.*, 2016).

In addition, other minor problems were found, but they would not be able to directly interfere with the results of the studies, since domains such as lack of results and evaluation of results were well described, as recommended by the evaluation tool. In this sense, none of the articles included in this review reached the maximum quality criteria, but there was also no work identified as having low quality (high risk of bias), all of which were classified as having “some problems” (figure 2). These results indicate that, although the studies did not meet all the quality criteria, this was possible in most domains, which enables a direct relationship with positive results between the practice of PE and the reduction of the clinical condition of GAD in individuals adults (HIGGINS *et al.*, 2016).

CONCLUSION

These results indicate that, although the analyzed studies did not unanimously reach all the quality criteria, this summary of this category points to the practice of PE as a tool with great potential to contribute to the treatment of GAD in adults.



This improvement in the state of exacerbated anxiety and in the State-Trait of Anxiety, for example, is possibly related to a practice of physical exercises of moderate intensity, regardless of the type of exercise (aerobic or anaerobic). However, it is important to emphasize that future investigations are necessary, and that these seek to clarify in more detail the physiological mechanisms and especially the neuroendocrine ones, by which such improvement in the clinical condition of GAD is promoted.

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AUTHORS' CONTRIBUTION

DOM, and MGC contributed equally to the elaboration of the manuscript. DOM and MGC designed the study and carried out the searches, data extraction, quality assessment, data compilation, analysis and discussion of the results and the general preparation of the manuscript. EO provided general guidance for carrying out the work, focusing on revisions, analysis and discussion of the results, as well as on the preparation and final revision of the manuscript.

CONFLICT OF INTEREST DECLARATION

This manuscript was self-funded by the authors and there is no conflict of interest regarding commercial and financial aspects between the authors.

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APPENDIX - FOOTNOTE

11. Coordenação de Aperfeiçoamento do Pessoal do Ensino Superior (CAPES).

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¹ Graduated in Physical Education – Universidade Federal do Pará (UFPA).

² PhD in Tropical Diseases and Professor and Researcher at the Universidade do Estado do Pará (UEPA).

³ PhD in Theory and Research of Behavior. Professor and Researcher at the Instituto Federal do Amapá – IFAP.

⁴ PhD in Tropical Diseases. Professor and Researcher at the Universidade Federal do Amapá, AP. Collaborating Researcher at the Núcleo de Medicina Tropical da UFPA (NMT-UFPA).

⁵ PhD in Psychology and Clinical Psychoanalysis. Doctorate in progress in Communication and Semiotics at the Pontifícia Universidade Católica de São Paulo (PUC/SP). Master's Degree in Religious Sciences from Universidade Presbiteriana Mackenzie. Master in Clinical Psychoanalysis. Degree in Biological Sciences. Degree in Theology. He has been working with Scientific Methodology (Research Method) for more than 15 years in the Scientific Production Guidance of



Master's and Doctoral Students. Specialist in Market Research and Health Research. ORCID: 0000-0003-2952-4337.

⁶ Master in Anthropogenic Studies in the Amazon – Programa de Pós-Graduação em Estudos Antrópicos na Amazônia (PPGEAA/UFPA) and Researcher – Grupo de Pesquisa em Saúde, Sociedade e Ambiente (GPSSA/UFPA).

⁷ PhD in Electrical Engineering. Lecturer and Researcher at the Universidade Federal do Pará – UFPA.

⁸ Doctor in Electrical Engineering. Lecturer and Researcher at the Universidade Federal do Pará – UFPA.

⁹ PhD in Science: Socio-environmental Development. Lecturer and Researcher at the Núcleo de Autos Estudos Amazônicos at the Universidade Federal do Pará – NAEA/UFPA.

¹⁰ PhD in Medicine/Tropical Diseases. Lecturer and Researcher at the Universidade Federal do Pará – UFPA. Collaborating Researcher at the Núcleo de Medicina Tropical – NMT/UFPA, Belém (PA), Brazil.