Trends in Psychiatry and Psychotherapy

Review Article

Can physical exercise modulate cortisol level in subjects with depression? A systematic review and meta-analysis

O exercício físico pode modular os níveis de cortisol em indivíduos com depressão? Uma revisão sistemática e metanálise

Ana Heloisa Nascimento Beserra,[1,2] Priscila Kameda,[1,2] Andrea Camaz Deslandes,[1,2] Felipe Barreto Schuch,[3] Jerson Laks,[1,4] Helena Sales de Moraes[1,2]

Abstract

Introduction: Major depressive disorder (MDD) is a prevalent medical illness that is associated with chronic stress. Patients with MDD can show an imbalance in cortisol levels, which can be restored with the remission of symptoms. Physical exercise training has been used as a tool to promote changes in cortisol levels in healthy individuals. However, it is unknown if exercise can produce the same results in individuals with MDD.
Objective: To review evidence of cortisol changes after exercise training in individuals with MDD.
Methods: We conducted a search on PubMed, SciELO, LILACS, ISI Web of Knowledge, Scopus, and PsycInfo databases. Random effects meta-analysis was performed and standardized mean difference (SMD) effect size was calculated. Analyses of forest and funnel plots was conducted using Stata v.11.0 software.
Results: At first, 463 studies were obtained in the search. After completion of the selection procedure, five articles with seven analyses were included. Type of exercise, frequency of training, cortisol measurement, and type of control group were analyzed. There was a reduction of cortisol levels in the exercise group (SMD = -0.65, 95%CI 1.30-0.01). Moreover, sensitivity analysis and subgroup analyses revealed an effect of type (aerobic exercise) and frequency (five times per week) of exercise on reduction of cortisol levels. However, these results should be interpreted cautiously due to the small number of studies and a substantial heterogeneity among them.
Conclusion: Physical exercise promotes a reduction in cortisol levels in individuals with MDD. However, this finding can be influenced by type of exercise, weekly frequency, and type of cortisol measurement.
Keywords: Physical activity, depression, cortisol, HPA axis, exercise.

Resumo

Introdução: A depressão maior (DM) é uma doença associada ao estresse crônico que pode apresentar um desequilíbrio nos níveis de cortisol, podendo ser recuperado com a remissão dos sintomas. O exercício tem sido utilizado como uma ferramenta para promover mudanças nos níveis de cortisol em indivíduos saudáveis. No entanto, não se sabe se o exercício produz os mesmos resultados em indivíduos com DM.
Objetivo: Revisar evidências de alterações dos níveis de cortisol após o exercício em indivíduos com DM.
Métodos: Foi realizada busca nas bases de dados PubMed, SciELO, LILACS, ISI Web of Knowledge, Scopus e PsycInfo. Procedeu-se a metanálise com o cálculo do tamanho do efeito da diferença de média padronizada. Foi utilizado o software Stata v.11.0.
Resultados: Foram obtidos na busca 463 estudos. Após o procedimento de seleção, cinco artigos com sete análises foram incluídos. O tipo de exercício, frequência de treinamento, tipo de medida do cortisol e tipo de grupo controle foram analisados como subgrupos. Houve uma redução dos níveis de cortisol no grupo de exercício. Além disso, a análise de sensibilidade e análises de subgrupos revelaram um efeito do tipo (exercício aeróbico) e da frequência (cinco vezes por semana) de exercício na redução dos níveis de cortisol. No entanto, esses resultados devem ser interpretados com cautela, devido ao pequeno número de estudos e uma heterogeneidade substancial entre eles.
Conclusão: O exercício promove redução dos níveis de cortisol em indivíduos com DM. No entanto, esse achado pode ser influenciado pelo tipo de exercício, medida do cortisol e frequência semanal.
Descritores: Atividade física, depressão, cortisol, eixo HPA, exercício.

[1] Instituto de Psiquiatria, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil. [2] Laboratório de Neurociência do Exercício (LaNEx), UFRJ, Rio de Janeiro, RJ, Brazil. [3] Centro Universitário La Salle, Canoas, RS, Brazil. [4] Programa de Pós-Graduação em Biomedicina Translacional, Universidade do Grande Rio (Unigranrio), Duque de Caxias, RJ, Brazil.

Submitted Dec 20 2017, accepted for publication May 03 2018.

Suggested citation: Beserra AHN, Kameda P, Deslandes AC, Schuch FB, Laks J, Moraes HS. Can physical exercise modulate cortisol level in subjects with depression? A systematic review and meta-analysis. Trends Psychiatry Psychother. 2018;40(4):360-368. http://dx.doi.org/10.1590/2237-6089-2017-0155

Introduction

Major depressive disorder (MDD) is a prevalent medical illness that comprises a variety of different symptoms (e.g., depressed mood, anhedonia, changes in appetite and sleeping, loss of energy, somatic symptoms and others).[1] The pathophysiology of MDD is related to several neurobiological changes, including hypothalamic-pituitary-adrenal (HPA) axis malfunction and consequent increase[2-4] or decrease[5-7] in basal cortisol levels. Previous studies have shown that pharmacological treatment can modulate cortisol levels independently of promoting remission of depressive symptoms.[8-10] Although drug therapy is the most common treatment for MDD, alternative treatments have been used in research as well as in clinical practice, mainly due to response failure to drug treatment.[11-13]

Previous studies have investigated the effect of physical exercise training on MDD and significant reduction of depressive symptoms has been found.[14-16] A meta-analysis reinforced that physical exercise is an effective non-pharmacological treatment for depression in older adults.[17] There are several physiological hypotheses to explain the positive effect of exercise on MDD, including HPA changes.[18,19] Physical exercise can modulate cortisol levels after a single session of exercise or after physical exercise training,[20] possibly due to an upregulation of glucocorticoid receptor.[21] However, it is still unknown whether exercise training might promote the same cortisol effects in individuals with MDD.

A previous article suggested that mindful exercise involving body movement and breathing can reduce stressful signals to the limbic system and thus HPA activity, resulting in reduced release of adrenal glucocorticoid.[22] Likewise, this hypothesis might be extrapolated to other types of exercise. A previous study from our laboratory showed that the differences in basal cortisol between MDD and healthy control groups can be modulated by physical performance aspects.[23] However, although the association between HPA malfunction and MDD has been investigated for five decades,[24] few interventional studies have evaluated the effect of physical exercise on cortisol levels in individuals with MDD, and the few results available are contradictory. Some studies have observed significant effect after aerobic training[25,26] or holistic training,[27,28] while others have shown non-significant changes after strength or aerobic training[29,30] or holistic activities.[31-33]

Therefore, the aim of the present study was to systematically review the literature investigating the effects of physical exercise training on cortisol levels in subjects with MDD and to explore potential moderators of this relationship. It is expected that physical exercise has an important effect on cortisol levels in individuals with MDD.

Methods

Protocol and registration

This study was registered on the International Prospective Register of Systematic Reviews (PROSPERO) under protocol no. CRD42018055996.

Eligibility criteria

The present systematic review and meta-analysis was conducted according to the PICO search strategy[34] and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[35] Our search permitted the selection of studies conducted in any country and reported in any language. Studies published anytime up to the day of the search (March 02 2018) were considered.

The inclusion criteria were randomized and controlled studies that investigated the effects of exercise training on cortisol levels in individuals with MDD compared to a control group. Also, MDD was defined through the use of established cut-offs for depression screening instruments (e.g., Geriatric Depression Scale [GDS], Center for Epidemiological Scale Depression [CES-D]) or diagnosed using structured or semi-structured diagnostic interviews (e.g., instruments based on criteria from the Diagnostic and Statistical Manual of Mental Disorders [DSM] or the International Classification of Diseases [ICD]). Control groups consisted of sedentary, no exercise, usual routine care, or relaxation.

Information sources

Two investigators (AHNB, PK) conducted a computer search on the PubMed, SciELO (Scientific Electronic Library), LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde), ISI Web of Knowledge (Institute for Scientific Information), Scopus, and PsycInfo databases. Studies published anytime up to March 02 2018 were included.

Search

The search strategy was performed using a combination of the keywords "exercise" AND "cortisol" AND "depression" with the descriptors "physical activity" AND "major depression". The details of the search were as follows: ("exercise" [All Fields] AND "cortisol" [All Fields] AND "depression" [All Fields]). Mesh terms: ("depressive disorder" [MeSH Terms] OR ("depressive" [All Fields] AND "disorder" [All Fields]) OR "depressive disorder" [All Fields] OR "depression" [All Fields] OR "depression" [MeSH Terms]) AND ("exercise" [MeSH Terms] OR "exercise" [All Fields]) AND ("hydrocortisone" [MeSH Terms] OR "hydrocortisone" [All Fields] OR "cortisol" [All Fields]). In some databases, filters were added for "Human" and "Clinical Trial" (PubMed) and "Document type" (Scopus and PsycInfo).

Study selection

Two investigators (AHNB, PK) selected the articles potentially eligible based on the analysis of the title (first selection) and abstract (second selection). Studies meeting any of these criteria were excluded: duplicate studies; studies with animal models; no original data (e.g., reviews); no control group; including patients with other clinical comorbidities (such as cancer, rheumatoid arthritis, alcohol dependence, other psychiatric disorders); evaluating dexamethasone response or acute effects (a single bout of exercise); or no data reported (mean and standard deviation). The full texts of the studies selected were evaluated independently and the meta-analysis was performed.

Data collection process

Two authors (AHNB, HSM) extracted the data from each study and entered them into a table with the following information: sample (age group, sex, clinical diagnosis), exercise method (type, intensity and duration of physical activity), cortisol method (type and time of collection), cortisol levels, and depressive symptoms.

Risk of bias in individual studies

Risk of bias was assessed according to the Physiotherapy Evidence Database (PEDro) scale,[36] considering the following items: eligibility criteria; subjects were randomly allocated to groups; allocation was concealed; the groups were similar at baseline regarding the most important prognostic indicators; there was blinding of all subjects; there was blinding of all therapists who administered the therapy; there was blinding of all assessors who measured at least one key outcome; measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by intention to treat; the results of between-group statistical comparisons are reported for at least one key outcome; and the study provides both point measures and measures of variability for at least one key outcome The score of this scale can range from 0 to 10 (yes = 1; no = 0). The first item was not included in the total score. Studies were considered to be of good quality when a score of 6 to 8 was reached, of moderate quality when the score was 4 to 5, and of poor quality when the score was below 3.

Statistical analysis

We performed a random effects meta-analysis and estimated the effect size using standardized mean differences (SMD). The SMD was calculated considering as continuous variables the mean and standard deviation of cortisol level post-intervention in each group (intervention and control) for each study. Analyses were performed using the Stata v.11.0 software, incorporating fixed- and random-effects assumptions. Fixed- and random-effects analyses did not yield different results; therefore, only the results of the random-effects analyses are here reported, as in this type we considered mostly the heterogeneity of the studies.

Heterogeneity was analyzed according to Higgins & Green,[37] i.e., I^2 statistics under 40% suggest that the heterogeneity among studies may not be important, whereas values over 75% indicate considerable heterogeneity. Estimates with p-values $\leq$ 0.05 were considered statistically significant. We used the scale suggested by Hopkins et al.[38] to interpret the data, according to the following classification: < 0.20, trivial; 0.20-0.60, small; 0.61-1.20, moderate; 1.21-2.00, large; 2.01-4.00, very large; > 4.00, almost perfect. Forest plots were used to present our main findings, and funnel plots, potential publication bias and afterward sensitivity analysis. We also performed subgroup analyses considering the heterogeneity of the studies, including: type of exercise, frequency of training, cortisol measurement, and type of control group.

Results

Systematic review

Study selection

At first, 463 studies were obtained in the search considering exercise, cortisol, and depression. Following application of the eligibility criteria, 24 studies were selected for full-text reading and review. After the selection procedure, five studies, with seven arms, were included in the meta-analysis. The selection process of the five studies[25,26,29,30,39] included in this meta-analysis is showed in Figure 1.

Study characteristics

Overall, the five studies included 209 participants (125 intervention vs. 84 control subjects). Three of the five studies used clinical diagnosis based on DSM-

IV or ICD-10 criteria, and the other two investigated depression using scales (GDS and CES-D). The mean age of the individual populations varied from 18.7±0.2 to 81.0±1.7 years old.

All the studies included were randomized controlled trials (Table 1). The duration of the intervention varied from 8 to 16 weeks for chronic studies. Different types of exercise were used, including aerobic exercise,[25,29,30]

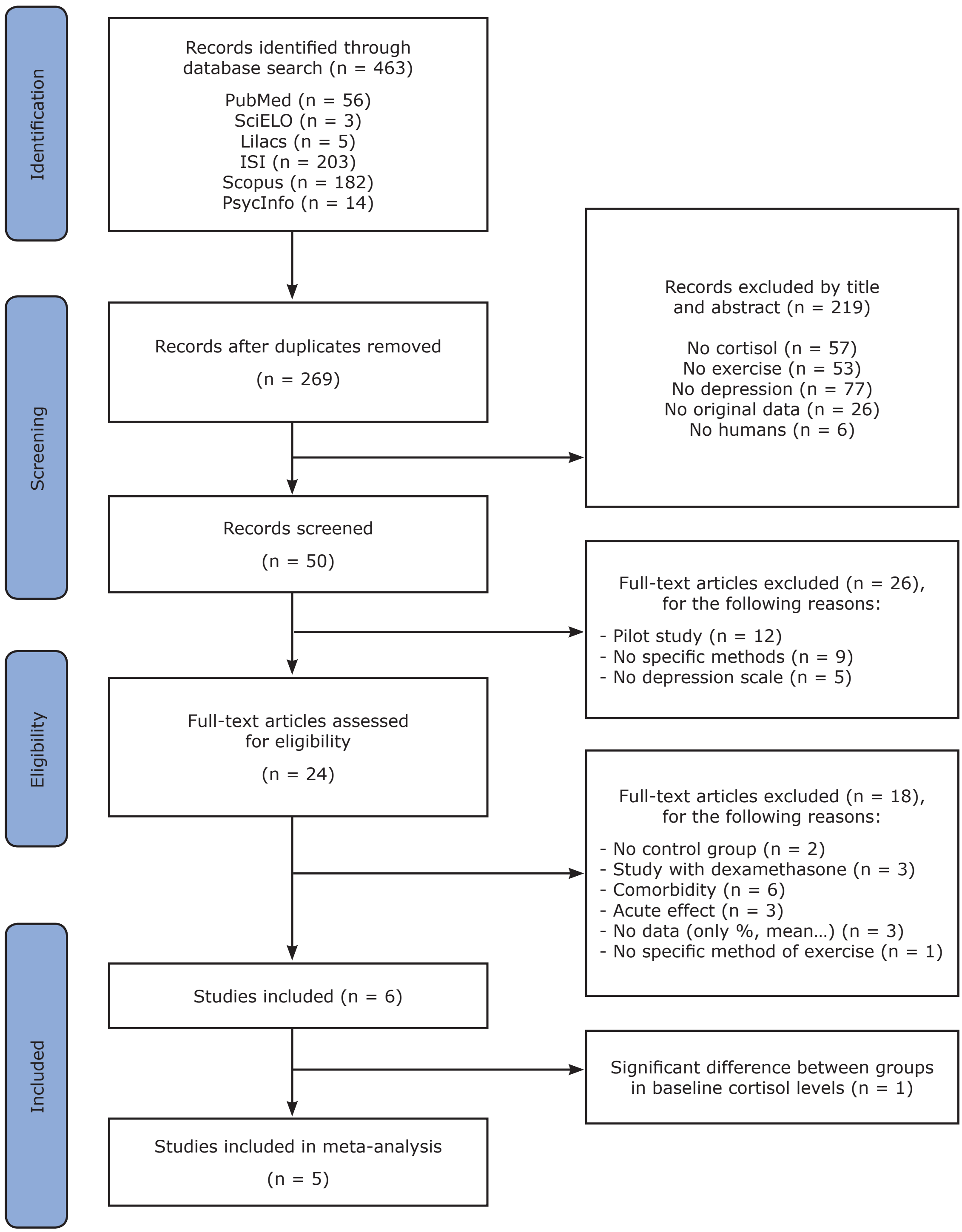

Figure 1 - Flowchart of study selection.

jogging training,[26] strength training,[29] relaxation exercise,[29] Buddhism walking meditation,[37] traditional walking[39] and stretching.[25]

Exercise intensity was also different among the studies. One study assessing strength training investigated 75% of repetition maximum (RM),[29] while the studies employing aerobic training used exercises of both high intensity[29] (n = 1) and mild to moderate intensity (n = 4).[25,26,30,39]

Cortisol measurement was made in the saliva (n = 1),[25] urine (n = 1),[26] and plasma (n = 3)[29,30,39] of the participants, at different times of the day. Cortisol assessments were also different among the studies. Two of them evaluated cortisol in basal condition,[29,30] one article observed cortisol awakening response,[25] another study assessed cortisol levels after 8 hours of overnight fasting[39] and the last one measured 24 hours of excretions.[26]

Meta-analysis

Primary findings

There was a moderate favorable effect of exercise training on reduction of cortisol levels (SMD = -0.65; 95% confidence interval [95%CI] -1.30 to 0.01) (Figure 2).

Risk of bias across studies

Visual analysis of the funnel plot showed asymmetry of two articles[26,29] (three trials) within the studies,

Table 1 - Summary of studies

Study	Sample characteristics	MD characteristics	Clinical diagnosis	Exercise type	Exercise methodology	Exercise intensity	Cortisol analysis	Cortisol measurement	Results
Foley et al.[25]	IG1 (n = 8), 18-55 years, male and female CG (n = 5), 18-55 years, male and female	IG1: BDI-II 21.40±4.33 MADRS 28.80±9.86 IG2: BDI-II 20.00±7.08 MADRS 28.69±8.59	DSM-IV	IG1: aerobic IG2: stretching	3 days per week, 30/40 minutes (6 and 12 weeks)	IG1: moderate IG2: mild	Saliva	Cortisol awakening response: awakening (T1), 30-minute post awakening (T2) and before bed (T3).	Cortisol: ↓ IG1 DS: ↓ IG1
Nabkasorn et al.[26]	IG1 (n = 21), 18.7±0.2 years, female CG (n = 28), 18.8±0.1 years, female	IG1: CES-D 20.1±0.9 IG2: CES-D 18.8±0.7	None	IG1: jogging then usual routine IG2: usual routine then jogging	IG1: 5 days per week, 50 minutes (8 weeks) IG2: 8 weeks	Mild; constant HR of less than 50% of the HR reserve	Urine	24 hours of excretions	Cortisol: ↓ after exercise for IG1 DS: ↓ after exercise for IG1 and IG2
Krogh et al.[29]	IG1 (n = 29), 42.4±9.5 years, male and female IG2 (n = 31), 39.3±9.8 years, male and female CG (n = 28), 36.0±9.8 years, male and female	IG1: HAM-D 17.6±3.5 IG2: HAM-D 18.4±4.2 CG: HAM-D 15.6±3.4	ICD-10	IG1: strength IG2: aerobic CG: relaxation	2 days per week, 60 minutes (16 weeks)	IG1: 50% of RM then 75% of RM IG2: % HR maximum from 70 to 90%	Plasma	Baseline (T1), post-intervention (T2)	Cortisol: NS DS: NS
Carneiro et al.[30]	IG (n = 9), 18-65 years, female CG (n = 10), 18-65 years, female	No scales	ICD-10	IG: aerobic CG: no exercise	3 days per week, 45/50 minutes (16 weeks)	Average intensity, 72% HR maximum	Plasma	Baseline (T1) and after 16 weeks (T2)	Cortisol: NS DS: -
Prakhinkit et al.[37]	IG1 (n = 13), 74.8±1.7 years, female IG2 (n = 14), 74.0±1.9, female CG (n = 13), 81.0±1.7, female	IG1: GDS 17.3±1.0 IG2: GDS 16.8±0.9 CG: GDS 17.9±0.7	None	IG1: traditional walking IG2: walking meditation CG: sedentary group	P1 (IG1 and IG2): 3 days per week, 20 minutes (weeks 1-6) P2 (IG1 and IG2): 3 days per week, 30 minutes (weeks 7-12)	P1 (IG1 and IG2): mild (20-39% HR reserve) P2 (IG1 and IG2): moderate (40-50% HR reserve)	Plasma	After 8 hours of overnight fasting	Cortisol: ↓ IG2 DS: ↓ IG2

BDI = Beck Depression Inventory; CES-D = Center for Epidemiological Scale Depression; CG = control group; DS = depressive symptoms; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th edition; GDS = Geriatric Depression Scale; HAM-D = Hamilton Depression Scale; HR = heart rate; ICD-10 = International Classification of Diseases; IG = intervention group; MADRS = Montgomery-Asberg Depression Rating Scale; MD = major depression; NS = non-significant; P = phase; RM = repetition maximum.

located outside the cone or as pseudo 95%CI. The plot is available in Online-Only Supplementary Figure 1.

Risk of bias within studies

Most studies included in this meta-analysis were classified as good quality (results available in Online-Only Supplementary Table 1).

Sensibility analysis

We performed a sensitivity analysis excluding the two trials that were located outside the funnel plot. The recalculated effect was equal to -0.64 (95%CI -1.17 to -0.10; I^2 = 28.7) (Table 2).

Subgroup analysis

Subgroup analyses are presented in Table 2. Significant reduction in cortisol levels was found for aerobic training (SMD = -0.76; 95%CI -1.55 to 0.03), while no effects were found for strength training (SMD = -0.05; 95%CI -0.57 to 0.47) (Online-Only Supplementary Figure 2).

A very large and significant reduction was found for exercising five times per week (SMD = -2.18; 95%CI -2.90 to -1.47), a moderate reduction for exercising three times per week (SMD = -0.64; 95%CI -1.17 to -0.10), and non-significant effects were found for exercising twice a week (SMD = 0.05; 95%CI -0.32 to 0.41) (Online-Only Supplementary Figure 3).

Regarding cortisol measurement, large effects were observed only for urine measurements (SMD = -2.18; 95%CI -2.90 to -1.47). Moderate but non-significant effects were found for cortisol measured in saliva (SMD = -0.88; 95%CI -2.06 to 0.30). Plasma measurement detected only a small reduction (SMD = -0.26; 95%CI -0.71 to -0.18) (Online-Only Supplementary Figure 4).

Finally, analysis of types of control groups revealed a trivial reduction of SMD when active treatment was used (SMD = -0.05; 95%CI -0.46 to 0.35), compared to a moderate reduction when the control group was not subjected to any treatment (SMD = -0.99; 95%CI -1.95 to -0.44) (Online-Only Supplementary Figure 5).

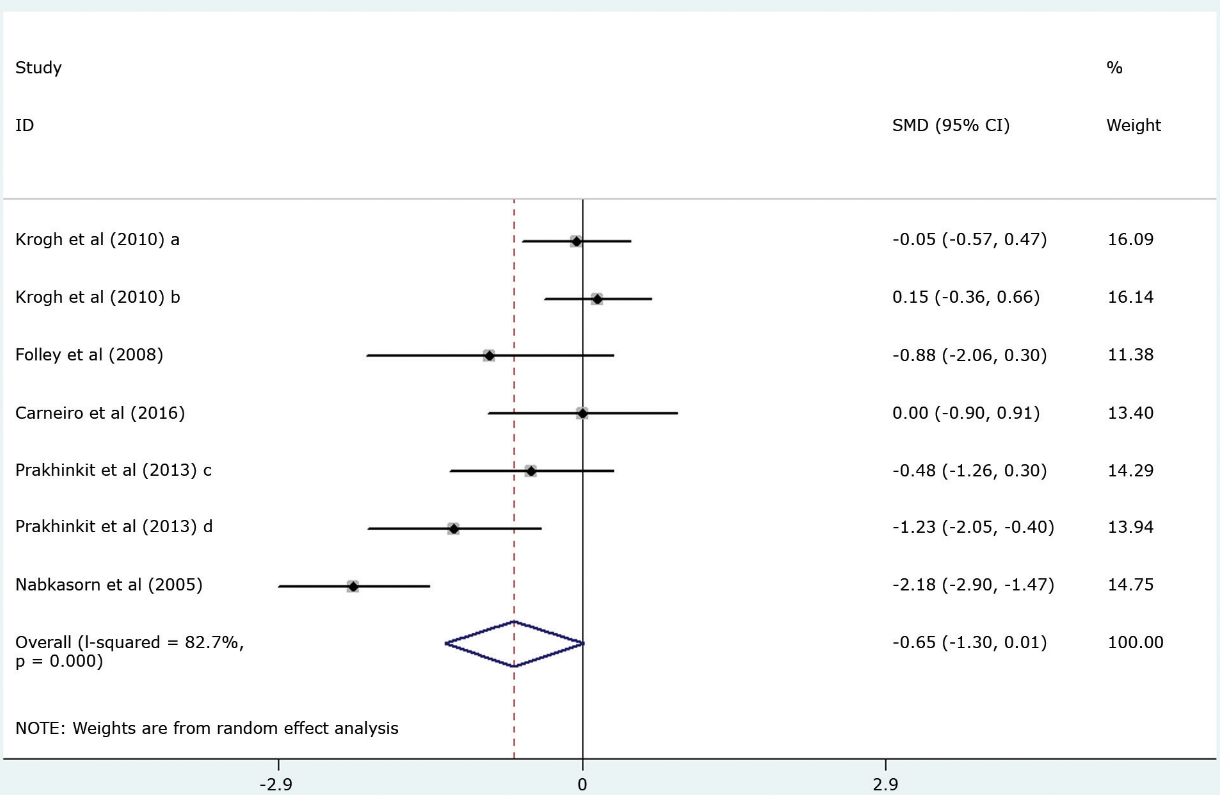

Figure 2 - Forest plot considering all the studies included in the meta-analysis.

Discussion

The current systematic review and meta-analysis aimed to synthesize the data available on cortisol changes after exercise training in individuals with MDD compared to control groups. A moderate reduction of cortisol levels was found following an exercise intervention in people with depression. However, these results should be interpreted cautiously due to the small number of studies and a substantial heterogeneity among them considering type of exercise, type of cortisol measurement, frequency of exercise, and type of control group.

Related to the type of exercise, the great majority of studies investigated aerobic exercise.[25,26,29,30,39] Strength training[29] and holistic exercise (walking meditation)[39] were also evaluated. Although a higher effect was observed for aerobic training, this result did not reach statistical significance, probably due to the small number of articles included in this meta-analysis. Moreover, the results were divergent. One study[29] observed non-significant reduction of cortisol after both aerobic and strength training. Another study[30] also observed non-significant differences in cortisol levels. It is interesting to note that these studies investigated cortisol at baseline conditions. However, studies which have observed cortisol awakening response,[25] morning cortisol after overnight fasting,[39] and 24 hours of excretion through urine[26] have found significant cortisol reductions. Since changes in diurnal rhythms of cortisol are well known to occur in some cases of MDD[40] and can vary according to time of sampling,[3] cortisol should be measured at different points of the day or in response to stimuli (awakening response or stressor) to produce remarkable results.

Another possible reason to explain the wide variability of the results is the type of specimen collection used to measure cortisol. Although a previous meta-analysis has concluded that this factor does not appear to impact the magnitude of change in cortisol levels pre- vs. post-treatment,[41] we observed a very large effect for urine, following by a moderate effect for saliva and a small effect for plasma. Plasma measurement is a widely used method, however it is the most invasive form when compared to saliva and urine collections (i.e., a stressful procedure). It is possible that 24-hour urine measures have the advantage of providing integrative HPA axis measures over larger time periods. Nonetheless, compliance is poor for 24-hour measures, and renal conditions may affect urinary cortisol levels.[42] In our meta-analysis, only one study evaluated this method.

Especially with regard to exercise methodology, the studies were also very discrepant, which may have impacted the results. For example, three different types of weekly frequencies were used: two,[29] three[25] and five times per week.[26] In our study, a very large effect was found for training when the frequency was five times

Table 2 - Subgroup meta-analyses

Analysis	SMD	95%CI	p	Heterogeneity	I² p
Main analysis (all trials)	-0.65	-1.30 to 0.01	0.054	82.7	<0.001
Main analysis (four trials)	-0.64	-1.17 to -0.10	0.019	28.7	0.240
Aerobic × strength					
Aerobic	-0.76	-1.55 to 0.03	0.059	83.9	<0.001
Strength	-0.05	-0.57 to 0.47	0.842	-	-
5, 3 or 2 times per week					
5 times per week	-2.18	-2.90 to -1.47	<0.001	-	-
3 times per week	-0.64	-1.17 to -0.10	0.019	28.7	0.240
2 times per week	0.05	-0.32 to 0.41	0.793	0.0	0.590
Saliva × plasma × urine					
Saliva	-0.88	-2.00 to 0.30	0.143	-	-
Plasma	-0.26	-0.71 to 0.18	0.249	53.8	0.070
Urine	-2.18	-2.90 to -1.47	<0.001	-	-
Control group types					
Active treatment	-0.05	-0.46 to 0.35	0.795	19.2	0.290
No treatment	-0.99	-1.95 to -0.04	0.042	82.4	<0.001

95%CI = 95% confidence interval; SMD = standardized mean difference.

a week, whereas a moderate effect was present for three times a week and a small effect for two times a week. Other parameters should be considered, such as exercise intensity, which can impact the weekly calorie expenditure and promote greater effects in depressive symptoms.[43] However, due to the heterogeneity of intensity measurement, we were not able to specifically evaluate dose response.

The variability of activities in the control groups was also an important methodological problem observed in the studies. For example, two studies[25,29] investigated an active control group (stretching and relaxation, respectively), while three studies[26,30,39] investigated a non-active control group. Our results indicate that a non-active control group, without any type of intervention or exercise, yields larger effect sizes when compared with control groups also subjected to exercise, as an active control group can present changes in cortisol levels even with interventions that do not involve physical exercise, e.g. relaxation techniques. For example, two researches[27,44] observed a significant reduction of cortisol levels using a deep breathing technique. Perhaps such holistic techniques can promote HPA changes through the reduction of negative cognitive and affective signals to the limbic system.[22]

Some limitations and strengths of the current meta-analysis should be considered. First, it is not possible to conclude that the effect of exercise on cortisol in individuals with MDD occurs concomitantly with reductions in depressive symptoms. Among the studies here evaluated, three showed significant reductions of depressive symptoms. However, one study did not present the association between reduced cortisol and improved depressive symptoms,[30] and another found non-significant results.[29] Second, our meta-analysis involved patients with a clinical diagnosis of depression and individuals with depressive symptoms according to depression scales. Due to the small number of articles included and the methodological differences among them, we cannot conclude if there was an influence of clinical diagnosis in the effect of exercise on cortisol levels. Finally, the small number of articles did not allow to reach a reliable conclusion regarding the subgroup analysis performed. Fortunately, most of the studies assessed in this meta-analysis were classified as good quality according to risk of bias within the studies. However, we assume that the quality of the trials published should be analyzed more cautiously.

Even though the findings of the present meta-analysis were not in accordance with the initial hypothesis, it is important to highlight that the modulation of cortisol in response to exercise training for depression needs to be investigated in more detail.

In conclusion, physical exercise promotes a moderate reduction in cortisol levels in MDD individuals. However, this finding can be influenced by methodological aspects, such as type of exercise, weekly frequency, and type of cortisol measurement.

Acknowledgements

Andrea Camaz Deslandes has received a fellowship from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; grant 301483/2016-7) and from Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ; grant E-26/203.193/2016).

Disclosure

No conflicts of interest declared concerning the publication of this article.

References

1. Parekh R. What is depression? [Internet] January 2017. [cited 2017 Dec 20]. https://www.psychiatry.org/patients-families/depression/what-is-depression
2. Gomez R, Fleming S, Keller J, Flores J, Kenna H, DeBattista C, et al. The neuropsychological profile of psychotic major depression and its relation to cortisol. Biol Psychiatry. 2006;60:472-8.
3. Murri MB, Pariante C, Mondelli V, Masotti M, Atti AR, Mellacqua Z, et al. HPA axis and aging in depression: systematic review and meta-analysis. Psychoneuroendocrinology. 2014;41:46-62.
4. Lopez-Duran NL, Kovacs M, George CJ. Hypothalamic-pituitary-adrenal axis dysregulation in depressed children and adolescents: a meta-analysis. Psychoneuroendocrinology. 2009;34:1272-83.
5. Gold PW, Chrousos GP. Organization of the stress system and its dysregulation in melancholic and atypical depression: high vs low CRH/NE states. Mol Psychiatry. 2002;7:254-75.
6. Chrousos GP. Stress and disorders of the stress system. Nat Rev Endocrinol. 2009;5:374-81.
7. Doolin K, Farrell C, Tozzi L, Harkin A. Diurnal hypothalamic-pituitary-adrenal axis measures and inflammatory marker correlates in major depressive disorder. Int J Mol Sci. 2017;18:2226.
8. Barden N. Implication of the hypothalamic-pituitary-adrenal axis in the physiopathology of depression. J Psychiatry Neurosci. 2004;29:185-93.
9. Vreeburg SA, Hoogendijk WJ, DeRijk RH, van Dyck R, Smit JH, Zitman FG, et al. Salivary cortisol levels and the 2-year course of depressive and anxiety disorders. Psychoneuroendocrinology. 2013;38:1494-502.
10. Fischer S, Macare C, Cleare AJ. Hypothalamic-pituitary-adrenal (HPA) axis functioning as predictor of antidepressant response - meta-analysis. Neurosci Biobehav Rev. 2017;83:200-11.
11. Brosse AL, Sheets ES, Lett HS, Blumenthal JA. Exercise and the treatment of clinical depression in adults: recent findings and future directions. Sports Med. 2002;32:741-60.
12. Blumenthal JA, Sherwood A, Rogers SD, Babyak MA, Doraiswamy PM, Watkins L, et al. Understanding prognostic benefits of exercise and antidepressant therapy for persons with depression and heart disease: the UPBEAT study – rationale, design, and methodological issues. Clin Trials. 2007;4:548-59.
13. Kok RM, Reynolds CF. Nonpharmacologic treatments for depression in older adults-reply. JAMA. 2017;318:1284.

14. Moraes, H, Deslandes A, Ferreira C, Pompeu FAMS, Ribeiro P, Laks J. O exercício físico no tratamento da depressão em idosos: revisão sistemática. Rev Psiquiatr Rio Gd Sul. 2007;29:70-9.
15. Deslandes AC, Moraes H, Alves H, Pompeu FAMS, Silveira H, Mouta R., et al. Effect of aerobic training on EEG alpha asymmetry and depressive symptoms in the elderly: a 1-year follow-up study. Braz J Med Bio Res. 2010:585-92.
16. Silveira H, Deslandes AC, de Moraes H, Mouta R, Ribeiro P, Piedade R, et al. Effects of exercise on electroencephalographic mean frequency in depressed elderly subjects. Neuropsychobiology. 2010;61:141-7.
17. Silveira H, Moraes H, Oliveira N, Coutinho ESF, Laks J, Deslandes A. Physical exercise and clinically depressed patients: a systematic review and meta-analysis. Neuropsychobiology. 2013;67:61-8.
18. Deslandes A, Moraes H, Ferreira C, Veiga H, Silveira H, Mouta R, et al. Exercise and mental health: many reasons to move. Neuropsychobiology. 2009;59:191-8.
19. Schuch FB, Deslandes AC, Stubbs B, Gosmann NP, Silva CTB, Fleck MPA. Neurobiological effects of exercise on major depressive disorder: A systematic review. Neurosci Biobehav Rev. 2016;61:1-11.
20. Moraes HS, Deslandes AC, Cevada T, Souza ACFM, Laks J. The effect of physical exercise on cortisol levels in older adults: a systematic review. Rev Bras Ativ Fis Saude. 2012;17:314-20.
21. Stranahan AM, Lee K, Mattson MP. Central mechanisms of HPA axis regulation by voluntary exercise. Neuromolecular Med. 2008;10:118-27.
22. Tsang HW, Fung KM. A review on neurobiological and psychological mechanisms underlying the anti-depressive effect of qigong exercise. J Health Psychol. 2008;13:857-63.
23. Moraes H, Deslandes A, Pinheiro PTM, Corrêa H, Laks J. Cortisol, DHEA: physical capacity. Arq Neuropsiquiatr. 2016;74:456-61.
24. Gibbons J, Mchugh P. Plasma cortisol in depressive illness. J Psychiatr Res. 1962;2:162-71.
25. Foley LS, Prapavessis H, Osuch EA, De Pace JA, Murphy BA, Podolinsky NJ. An examination of potential mechanisms for exercise as a treatment for depression: A pilot study. Ment Health Phys Activity. 2008:69-73.
26. Nabkasorn C, Miyai N, Sootmongkol A, Junprasert S, Yamamoto H, Arita M, et al. Effects of physical exercise on depression, neuroendocrine stress hormones and physiological fitness in adolescent females with depressive symptoms. Eur J Public Health. 2006;16:179-84.
27. Vedamurthachar A, Janakiramaiah N, Hegde JM, Shetty TK, Subbakrishna DK, Sureshbabu SV, et al. Antidepressant efficacy and hormonal effects of Sudarshana Kriya Yoga (SKY) in alcohol dependent individuals. J Affect Disord. 2006;94:249-53.
28. Chan ES, Koh D, Teo YC, Hj Tamin R, Lim A, Fredericks S. Biochemical and psychometric evaluation of Self-Healing Qigong as a stress reduction tool among first year nursing and midwifery students. Complement Ther Clin Pract. 2013;19:179-83.
29. Krogh J, Nordentoft M, Mohammad-Nezhad M, Westrin A. Growth hormone, prolactin and cortisol response to exercise in patients with depression. J Affect Disord. 2010;125:189-97.
30. Carneiro LS, Mota MP, Vieira-Coelho MA, Alves RC, Fonseca AM, Vasconcelos-Raposo J. Monoamines and cortisol as potential mediators of the relationship between exercise and depressive symptoms. Eur Arch Psychiatry Clin Neurosci. 2017;267:117-21.
31. Jorge MP, Santaella DF, Pontes IM, Shiramizu VK, Nascimento EB, Cabral A, et al. Hatha Yoga practice decreases menopause symptoms and improves quality of life: A randomized controlled trial. Complement Ther Med. 2016;26:128-35.
32. Sarubin N, Nothdurfter C, Schüle C, Lieb M, Uhr M, Born C, et al. The influence of Hatha yoga as an add-on treatment in major depression on hypothalamic-pituitary-adrenal-axis activity: a randomized trial. J Psychiatr Res. 2014;53:76-83.
33. Woolery A, Myers H, Sternlieb B, Zeltzer L. A yoga intervention for young adults with elevated symptoms of depression. Altern Ther Health Med. 2004;10:60-3.
34. Heneghan C, Badenoch D. Evidence-based medicine toolkit. London: BMJ Books; 2002.
35. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ann Intern Med. 2009; 151:65-94.
36. Sherrington C, Herbert RD, Maher CG, Moseley AM. PEDro. A database of randomized trials and systematic reviews in physiotherapy. Man Ther. 2000;5:223-6.
37. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions. Chichester: Wiley; 2008.
38. Hopkings WG, Marshall SW, Batterham AM, Hanin J. Progressive statistics for studies in sports medicine and exercise science. Med Sci Sports Exerc. 2009;41:3-13.
39. Prakhinkit S, Suppapitiporn S, Suksom D. Effects of Buddhism walking meditation on depression, functional fitness, and endothelium-dependent vasodilation in depressed elderly. J Altern Complement Med. 2014;20:411-6.
40. Herbert J. Cortisol and depression: three questions for psychiatry. Psychol Med. 2012;43:449-69.
41. McKay MS, Zakzanis KK. The impact of treatment on HPA axis activity in unipolar major depression. J Psychiatr Res. 2010;44:183-92.
42. Hellhammer DH, Wust S, Kudielka BM. Salivary cortisol as a biomarker in stress research. Psychoneuroendocrinology. 2009;34:163-71.
43. Dunn AL, Trivedi MH, Kampert JB, Clark CG, Chambliss HO. Exercise treatment for depression: efficacy and dose response. Am J Prev Med. 2005;28:1–8.
44. Perciavalle V, Blandini M, Fecarotta P, Buscemi A, Di Corrado D, Bertolo L, et al. The role of deep breathing on stress. Neurol Sci. 2017;38:451-8.

Correspondence:
Ana Beserra
Av. Venceslau Braz, 71, fundos, Botafogo
22290-140 - Rio de Janeiro, RJ - Brazil
Tel.: +55 (21) 39385546
E-mail: biomedica.anabeserra@gmail.com