SIENIAWSKA, Daria, SIENIAWSKA, Julia and PROSZOWSKA, Patrycja. The Impact of Physical Activity on Depression Treatment: A Literature Review. Quality in Sport. 2024;16:52858. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.16.52858
https://apcz.umk.pl/QS/article/view/52858

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 24.06.2024. Revised: 10.07.2024. Accepted: 12.07.2024. Published: 15.07.2024.

The Impact of Physical Activity on Depression Treatment: A Literature Review

Daria Sieniawska

University Clinical Hospital named after F. Chopin in Rzeszów, St. F. Chopin 2 35-055: Rzeszów, PL

sieniawska.daria@gmail.com

https://orcid.org/0009-0004-1019-6227

Julia Sieniawska

Rzeszów University, Al. Rejtana 16c 35-959 Rzeszów, PL

julia.sieniawska01@gmail.com

https://orcid.org/0009-0002-3737-5079

Patrycja Proszowska

University Clinical Hospital named after F. Chopin in Rzeszów, St. F. Chopin 2 35-055 Rzeszów, PL

proszowska.patrycja@gmail.com

https://orcid.org/0009-0005-5421-4009

Abstract

Introduction

Engaging in physical exercise can have a significant impact on the treatment of mild-to-moderate mental health conditions, including depression. Existing antidepressant medications have limited clinical effectiveness as they fail to achieve a complete response in around 30% of depressed patients and do not induce remission in these individuals. Physical exercise can enhance the effects of antidepressant therapy in individuals with depression by boosting the health of neurons and improving the responsiveness to medication.

Aim of the study

The aim of the study is to investigate the role of physical activity in in the management of mental health diseases, especially depression.

Materials and methods

This study represents the current state of knowledge about the antidepressant effects of physical activity, particularly in the context of depressive disorders. It presents a comprehensive overview of how regular exercise can serve as an effective therapeutic strategy for managing depressive symptoms. PubMed and Google Scholar database was searched for articles written in English. The search included the keywords.

Results

Regular exercise significantly alleviates depressive symptoms through various mechanisms. Exercise enhances the production of endorphins, which improve mood and reduce anxiety. It also influences neurotransmitter systems, including serotonin, dopamine, and norepinephrine, which are crucial in regulating mood and emotion. Additionally, physical activity stimulates the production of brain-derived neurotrophic factor (BDNF) and transforming growth factor-beta 1 (TGF-β1), both of which support neurogenesis and synaptic plasticity, contributing to improved cognitive function and mood stabilization.

Key words: „Depression”; “ Exercise”, „Physical activity”

Introduction

Depression is a significant condition that has similar clinical and social effects to chronic diseases including diabetes, congestive heart failure, and hypertension[1]. Depression, as defined by the World Health Organisation, is a medical condition marked by a pessimistic mood, reduced enjoyment in pleasurable activities, feelings of guilt, disrupted sleep, decreased food and energy, and impaired cognitive focus[2,3]. These emotions can manifest as either acute or persistent, leading to a diminished enthusiasm for life that may culminate in extreme measures like suicide[4]. The International Classification of Diseases (ICD-11) establishes the criteria for classifying depression on a global scale[5]. Major depressive disorder (MDD) is a prominent contributor to global disability[6] and has been shown to have a greater negative impact on life satisfaction compared to debt, divorce, and diabetes[7]. It also worsens the symptoms of other health conditions, such as heart disease[8], anxiety[9], and cancer[10]. While pharmacological therapies and psychotherapy are generally effective for individuals with major depressive illness, a significant number of patients exhibit resistance to these forms of treatment. The "monoaminergic hypothesis" has been originally confirmed by the creation of monoaminergic antidepressants, among several ideas presented to explain the pathophysiology of Major depressive disorder. According to this concept, a dysfunction of monoaminergic systems (serotonin, noradrenaline, and dopamine) has been identified as the main cause for the development of emotional and cognitive symptoms in Major Depressive Disorder[13]. Consequently, most antidepressant medications have been created based on this theory, making them a valuable treatment option[14]. Regrettably, around 30% of individuals suffering from depression are classified as treatment resistant[15]. This is likely due to the emergence of other variables that contribute to the development of Major Depressive Disorder, such as chronic stress and neuroinflammation, which should be taken into account[16].

Neurotransmitter deficiency hypothesis

Research conducted throughout the second half of the 20th century was significantly impacted by the finding that substances which modify the breakdown of monoamine neurotransmitters, specifically serotonin (5-hydroxytryptamine, 5-HT) and norepinephrine (NE), alleviated symptoms of depression. Both monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs) are nonselective drugs, meaning that they have a wide range of actions. As a result, their therapeutic advantages are accompanied with significant adverse effects. More recent and focused medications, such as selective serotonin reuptake inhibitors

(SSRIs) and NE reuptake inhibitors (NRIs), have proven to be beneficial in alleviating symptoms in a considerable proportion of patients. Despite the possibility of experiencing inconvenient side effects, these medications are often more easily tolerated compared to tricyclic antidepressants and monoamine oxidase inhibitors. However, the level of side effects may be significant enough to result in the termination of treatment in around 14.9% of patients receiving SSRI medication. This proportion is comparable to the 19% of individuals who discontinue treatment with tricyclic antidepressants in short-term trials. Despite 50 years of research and the availability of many drugs to treat major depressive disorder, the effectiveness of current medications is not sufficient, and no treatment is fully curative. Around 50% of patients with major depressive disorder do not respond to initial therapy, and over 65% do not achieve remission. Despite undergoing consecutive courses of medicine, a significant proportion of patients, ranging from 10% to 20%, fail to attain remission. However, an examination conducted after the fact of the data from the Sequenced Treatment Alternatives to Relieve Depression trial revealed that 90% of patients who successfully reached remission still experienced at least one lingering symptom. Certain symptoms, such as cognitive impairment, regularly exhibit a longer duration of resolution compared to mood symptoms and may endure for several years. What is perhaps more concerning than their continued presence is the finding that lingering symptoms were able to forecast a relapse, even in individuals who had satisfied the requirements for recovery during the initial episode[17].

The idea has received substantial support due to its attempt to give a pathophysiologic explanation for the effects of antidepressants. Nevertheless, in its initial state, it is evidently insufficient as it fails to offer a comprehensive elucidation for the effects of antidepressants, and the underlying mechanisms of depression remain elusive. The concept has developed over time to incorporate adaptive modifications in receptors, which aim to elucidate the reason behind the slow clinical response to antidepressant medication despite the fast rise in availability of monoamines. However, the monoamine hypothesis fails to explain important matters, such as the effectiveness of antidepressants in treating other conditions like panic disorder, obsessive-compulsive disorder, and bulimia. It also does not account for the fact that not all drugs that enhance serotonergic or noradrenergic transmission are effective in treating depression. Notwithstanding these constraints, it is evident that the advancement of the monoamine hypothesis has played a crucial role in comprehending sadness and in creating secure and efficient pharmaceutical substances for its management[18].

Changes in brain structure

Brain structural alterations in individuals with depression are strongly linked to certain components of the nervous system, such as the frontal lobe, cingulate gyrus, hippocampus, striatum, and white matter[19]. Depressive episodes are associated with reductions in brain volume, which include structural alterations such as neuronal death and reduced neurotrophic factor. The hippocampus is a crucial component in cognitive function, as well as the control of stress and mood in those suffering from depression. Research has indicated that individuals with depression may have noticeable decreases in the size of their hippocampus and experience poor emotional regulation[20,21]. In addition, a recent meta-analysis of 15 research revealed that individuals suffering from depression exhibited reduced volumes of the hippocampus. This reduction was more pronounced in those with early-onset depression (under the age of 21), perhaps leading to a longer duration of depression and a higher likelihood of recurrence. The authors posited that persistent stress resulted in elevated levels of glucocorticoids, together with malfunction of the hypothalamic-pituitary-adrenal axis, shrinkage of the hippocampus structure, and reduced neurogenesis, eventually resulting in depression[22]. Depression in adult patients may be caused by the deterioration of synaptic connections between neurons in the hippocampus. A postmortem examination revealed that individuals with depression had compromised plasticity of hippocampal neurons, characterised by a decline in the density of grey matter in the hippocampus, as well as a decrease in the connectivity of nerve fibres and the generation of new neurons in the hippocampus. Elderly persons with depression also see a decrease in the size of their hippocampus[23].

β-Endorphin and Exercise

Endorphins are natural opioid peptides that are synthesised by the pituitary gland and hypothalamus in vertebrates in response to intense physical activity, excitement, or pain. They have similar effects to opiates, such as pain relief and a feeling of happiness or contentment [24]. The opioid system has a significant function in facilitating pain relief and promoting social bonding. Additionally, it may have an impact on depression, since there is a connection between β-endorphins and symptoms of sadness [25]. Existing findings indicate that the μ-opioidergic system plays a significant role in the development of mental illnesses. This suggests that μ-opioid ligands, such as β-endorphin, might be used in behavioural therapy. The 'endorphins theory' suggests that exercise increases the release of naturally occurring

opioid peptides in the brain, leading to pain reduction and a state of overall bliss. Consequently, the latter reduces levels of anxiety and sadness [26].

A research examined the endorphins hypothesis in competitive long distance athletes, namely those who trained for more than 4 hours per week in the past 2 years. The study sought to elucidate the opioidergic processes behind the runner's high in the human brain and to establish the correlation with experienced bliss. Decreases in the availability of opioid receptors were seen mostly in prefrontal and limbic/paralimbic brain areas. Running greatly heightened the feeling of euphoria and showed a negative correlation with opioid binding in certain brain areas, including the prefrontal/orbitofrontal cortices, anterior cingulate cortex, bilateral insula, parainsular cortex, and temporoparietal regions. These findings support the endorphin theory, showing that exercise causes a higher release of endorphins, which results in improved mood states [27].

The Role of Neurotrophic Factors and the Possible Impact of Physical Activity

The pathophysiology of major depressive illness can be explained by chronic stress, decreased synaptic plasticity, impaired adult hippocampal neurogenesis, hippocampus neurodegeneration, and dysregulation of the monoaminergic system[28]. Epidemiological studies provide evidence for the significant impact of persistent stress on major depressive disorder[29]. Indeed, the occurrence of stressful life events is a contributing factor to the development of this illness [30]. Prolonged stress causes a disruption in the ability of glucocorticoids (GR) to regulate the activity of the Hypothalamic-Pituitary-Adrenal (HPA) Axis, leading to increased levels of cortisol [31]. An excessive amount of glucocorticoid receptor (GR) can cause cell death in the hippocampus and lead to abnormal alterations in the prefrontal cortex (PFC). These two brain areas play a crucial role in the cognitive symptoms of depression.

Antidepressant medications, such sertraline and fluoxetine, have immunomodulatory effects by decreasing the production of pro-inflammatory cytokines and promoting the synthesis of Transforming Growth Factor TGF-β1 in individuals with depression [34]. Moreover, research conducted both in laboratory settings (in vitro) and in living organisms (in vivo) has shown that certain antidepressant medications can stimulate the production and release of brain-derived neurotrophic factor (BDNF) and transforming growth factor beta 1 (TGF-β1). This suggests that the delay in BDNF restoration may partially account for the therapeutic latency (2-4 weeks) observed with these drugs. Research has shown that TGF-β1 has fast and enduring antidepressant effects. It has also been found that TGF-β1 secreted by microglia

plays a crucial role in the antidepressant action of (R)-ketamine in a mouse model of depression [37]. (R)-ketamine is being investigated as a potential therapy for people with treatment-resistant Major depressive disorder. Remarkably, this medication restored the presence of TGF-β1 and its receptors in the prefrontal cortex (PFC) and hippocampus. Conversely, when TGF-β1 signalling was inhibited or a neutralising antibody for TGF-β1 was used, the antidepressant effects of (R)-ketamine were prevented. This indicates that TGF-β1 plays a crucial and innovative role as an antidepressant.

A research done by Murri et al. has shown that engaging in physical exercise, together with the use of the SSRI sertraline, decreases emotional symptoms and slows down psychomotor activity in individuals with Major Depressive Disorder[38]. Engaging in physical exercise has positive benefits on brain development before and after birth[39]. It promotes the growth of new nerve cells and the ability of existing nerve cells to form connections by boosting the production and release of brain-derived neurotrophic factor (BDNF)[40]. Additionally, it helps to minimise excessive stimulation of the hypothalamic-pituitary-adrenal (HPA) axis[41]. It has been suggested that irisin, a protein produced during exercise by breaking down a membrane protein called FNDC5, may demonstrate a connection between muscles and the brain. Irisin is able to pass through the blood-brain barrier and has the potential to stimulate the expression of BDNF in the brain. This, in turn, could lead to an increase in the growth of new neurons in the hippocampus, resulting in improved learning, memory, and mood. In relation to TGF-β1, the level of this neurotrophin in the blood rises as a result of physical activity [43].

The research discussed above indicates that there is a synergistic impact when combining aerobic exercise (AE) with antidepressant medicines for treating depression. This combination helps to reduce the cognitive deficiencies that affect the ability of patients with major depressive disorder to do their daily tasks and also lowers their risk of relapse [44].

Aerobic Physical Activity versus Strength and Flexibility Training

Martinsen conducted a study to examine the impact of aerobic exercise compared to strength and flexibility training on depressive symptoms in hospitalised patients who matched the criteria for clinical depression. Both research groups saw substantial and comparable decreases in depression ratings as measured by the Montgomery-Åsberg Depression Rating Scale[45]. A different study examined the impact of different levels of activity on depressive scores, as measured by a General Health Questionnaire, for individuals who were not hospitalised. The study found that the actual activity itself had a greater effect in reducing

depressive symptoms compared to the cardiovascular fitness achieved through intense activity[46]. An additional research offered help by randomly assigning young women who satisfied the criteria for depression according to the Research Diagnostic Criteria (RDC) to one of three conditions: an 8-week jogging programme, an 8-week weight lifting programme, or a waiting condition[47]. The researchers determined that both exercise groups resulted in substantial decreases in depression, as measured by various methods, compared to the control group. Furthermore, they found that jogging and weight lifting caused similar benefits and could not be distinguished from one other.

The intensity and duration of exercise are crucial factors in using physical activity as a therapeutic measure. The significance of this result is underscored by a randomised intervention study including older people who were both healthy and sedentary. The scientists observed that a daily exercise plan with moderate intensity was just as successful as a more typical intermittent programme with high intensity in improving overall health[48]. Given that individuals with mental health illnesses may have an aversion to intense exercise routines, it is advisable to suggest a consistent and moderate intensity programme lasting 30 minutes on most days of the week. This approach is more likely to result in higher adherence and success rates.

In general, a significant number of the existing research on the relationship between depression and exercise have notable limitations. Their conclusions are limited due to the very small sample numbers, short research durations, and insufficient control groups. The lack of uniform definitions of depression, together with the use of various psychological measures, hinders the ability to generalise the findings of the investigations. However, both aerobic and nonaerobic physical activities appear to be advantageous for treating mild-to-moderate depression symptoms. Furthermore, exercise appears to have comparable effectiveness to psychotherapy and does not present any notable reasons to avoid the use of drugs. Further extensive, population-based, well regulated research are unquestionably necessary.

Conclusions

Although medication and psychotherapy are widely used, a significant proportion of patients still do not respond to these conventional treatments. This has led to the investigation of alternative or additional therapies. Engaging in regular physical exercise enhances mood and promotes general mental well-being, therefore establishing its efficacy as a useful treatment approach. Integrating exercise with antidepressant medication might improve the effectiveness of treatment, decreasing emotional symptoms and cognitive impairments that

contribute to the frequent recurrence of depression in individuals with Major Depressive Disorder (MDD). Both aerobic and nonaerobic workouts, including strength and flexibility training, have been proven to effectively reduce symptoms of depression. Engaging in physical exercise is a beneficial and effective method for controlling depression, providing benefits to both the body and mind. Integrating physical activity with conventional therapy methods for Major Depressive Disorder (MDD) might boost patient results, enhance quality of life, and perhaps alleviate the impact of this incapacitating condition. There is a requirement for extensive, well-regulated, and extended research to get a deeper understanding of the most effective forms, levels, and frequencies of physical activity that yield the greatest advantages in treating depression.

After conclusions

Author's contribution:

Conceptalization: Julia Sieniawska, methodology: Patrycja Proszowska, software, Daria Sieniawska, check: Patrycja Proszowska, formal analysis: Patrycja Proszowska, investigation: Julia Sieniawska, resources, Daria Sieniawska, data curation, Patrycja Proszowska, writing-rough preparation, Daria Sieniawska, visualization, Patrycja Proszowska, supervision, Julia Sieniawska, project administration, Daria Sieniawska

All authors have read and agreed with the published version of the manuscript

Disclosure

Funding statement

The study did not receive special funding.

Informed Consent Statement

Not applicable

Acknowledgments

Not applicable

Conflict of Interest Statement

The authors report no conflicts of interest.

References:

1. Katon WayneJ (2011) Epidemiology and treatment of depression in patients with chronic medical illness. Dialogues Clin Neurosci 13:7

2. Depression. https://www.who.int/health-topics/depression#tab=tab_1. Accessed 13 Jun 2024
3. Chand SP, Arif H (2023) Depression. StatPearls
4. Harmer B, Lee S, Rizvi A, Saadabadi A (2024) Suicidal Ideation. Acute Medicine: A Symptom-Based Approach 415–420
5. ICD-11 for Mortality and Morbidity Statistics. https://icd.who.int/browse/2024-01/mms/en. Accessed 13 Jun 2024
6. Depressive disorder (depression). https://www.who.int/news-room/fact-sheets/detail/depression. Accessed 13 Jun 2024
7. WALY Report | Happiness Resarch Institute. https://www.happinessresearchinstitute.com/waly-report. Accessed 13 Jun 2024
8. Rugulies R (2002) Depression as a predictor for coronary heart disease: A review and meta-analysis. Am J Prev Med 23:51–61
9. Jacobson NC, Newman MG (2017) Anxiety and depression as bidirectional risk factors for one another: A meta-analysis of longitudinal studies. Psychol Bull 143:1155–1200
10. Pinquart M, Duberstein PR (2010) Depression and cancer mortality: a meta-analysis. Psychol Med 40:1797–1810
11. Cuijpers P, Quero S, Noma H, Ciharova M, Miguel C, Karyotaki E, Cipriani A, Cristea IA, Furukawa TA (2021) Psychotherapies for depression: a network meta-analysis covering efficacy, acceptability and long-term outcomes of all main treatment types. World Psychiatry 20:283–293
12. Strawbridge R, Carter B, Marwood L, et al (2019) Augmentation therapies for treatment-resistant depression: systematic review and meta-analysis. The British Journal of Psychiatry 214:42–51
13. Hamon M, Blier P (2013) Monoamine neurocircuitry in depression and strategies for new treatments. Prog Neuropsychopharmacol Biol Psychiatry 45:54–63
14. Lopez-Munoz F, Alamo C (2009) Monoaminergic neurotransmission: the history of the discovery of antidepressants from 1950s until today. Curr Pharm Des 15:1563–1586
15. Caraci F, Calabrese F, Molteni R, et al (2018) International Union of Basic and Clinical Pharmacology CIV: The Neurobiology of Treatment-resistant Depression: From Antidepressant Classifications to Novel Pharmacological Targets. Pharmacol Rev 70:475–504
16. Caraci F, Spampinato SF, Morgese MG, et al (2018) Neurobiological links between depression and AD: The role of TGF-β1 signaling as a new pharmacological target. Pharmacol Res 130:374–384

17. Hamon M, Blier P (2013) Monoamine neurocircuitry in depression and strategies for new treatments. Prog Neuropsychopharmacol Biol Psychiatry 45:54–63
18. Hirschfeld RMA (2000) History and Evolution of the Monoamine Hypothesis of Depression. J Clin Psychiatry 61:8272
19. Zhang FF, Peng W, Sweeney JA, Jia ZY, Gong QY (2018) Brain structure alterations in depression: Psychoradiological evidence. CNS Neurosci Ther 24:994–1003
20. Campbell S, MacQueen G (2004) The role of the hippocampus in the pathophysiology of major depression. Journal of Psychiatry and Neuroscience 29:417
21. Geerlings MI, Gerritsen L (2017) Late-Life Depression, Hippocampal Volumes, and Hypothalamic-Pituitary-Adrenal Axis Regulation: A Systematic Review and Meta-analysis. Biol Psychiatry 82:339–350
22. Schmaal L, Veltman DJ, Van Erp TGM, et al (2016) Subcortical brain alterations in major depressive disorder: findings from the ENIGMA Major Depressive Disorder working group. Mol Psychiatry 21:806–812
23. Sexton CE, MacKay CE, Ebmeier KP (2013) A systematic review and meta-analysis of magnetic resonance imaging studies in late-life depression. Am J Geriatr Psychiatry 21:184–195
24. Fichna J, Janecka A, Costentin J, Do Rego JC (2007) The endomorphin system and its evolving neurophysiological role. Pharmacol Rev 59:88–123
25. Navinés R, Martín-Santos R, Gómez-Gil E, Martínez de Osaba MJ, Gastó C (2008) Interaction between serotonin 5-HT1A receptors and beta-endorphins modulates antidepressant response. Prog Neuropsychopharmacol Biol Psychiatry 32:1804–1809
26. Grisel JE, Bartels JL, Allen SA, Turgeon VL (2008) Influence of β-Endorphin on anxious behavior in mice: Interaction with EtOH. Psychopharmacology (Berl) 200:105–115
27. Boecker H, Sprenger T, Spilker ME, Henriksen G, Koppenhoefer M, Wagner KJ, Valet M, Berthele A, Tolle TR (2008) The runner's high: opioidergic mechanisms in the human brain. Cereb Cortex 18:2523–2531
28. Jaggar M, Fanibunda SE, Ghosh S, Duman RS, Vaidya VA (2019) The Neurotrophic Hypothesis of Depression Revisited: New Insights and Therapeutic Implications. Neurobiology of Depression: Road to Novel Therapeutics 43–62
29. Pittenger C, Duman RS (2008) Stress, depression, and neuroplasticity: a convergence of mechanisms. Neuropsychopharmacology 33:88–109

30. Czéh B, Lucassen PJ (2007) What causes the hippocampal volume decrease in depression? Are neurogenesis, glial changes and apoptosis implicated? Eur Arch Psychiatry Clin Neurosci 257:250–260

31. De Kloet ER, Joëls M, Holsboer F (2005) Stress and the brain: from adaptation to disease. Nat Rev Neurosci 6:463–475

32. Yu S, Holsboer F, Almeida OFX (2008) Neuronal actions of glucocorticoids: focus on depression. J Steroid Biochem Mol Biol 108:300–309

33. Krishnan V, Nestler EJ (2008) The molecular neurobiology of depression. Nature 455:894–902

34. Maes M, Nowak G, Caso JR, et al (2016) Toward Omics-Based, Systems Biomedicine, and Path and Drug Discovery Methodologies for Depression-Inflammation Research. Mol Neurobiol 53:2927–2935

35. Caraci F, Copani A, Nicoletti F, Drago F (2010) Depression and Alzheimer's disease: neurobiological links and common pharmacological targets. Eur J Pharmacol 626:64–71

36. Racagni G, Popoli M (2010) The pharmacological properties of antidepressants. Int Clin Psychopharmacol 25:117–131

37. Zhang K, Yang C, Chang L, et al (2020) Essential role of microglial transforming growth factor-β1 in antidepressant actions of (R)-ketamine and the novel antidepressant TGF-β1. Transl Psychiatry. https://doi.org/10.1038/S41398-020-0733-X

38. Murri MB, Ekkekakis P, Menchetti M, et al (2018) Physical exercise for late-life depression: Effects on symptom dimensions and time course. J Affect Disord 230:65–70

39. Gomes da Silva S, Arida RM (2015) Physical activity and brain development. Expert Rev Neurother 15:1041–1051

40. Walsh JJ, Tschakovsky ME (2018) Exercise and circulating BDNF: Mechanisms of release and implications for the design of exercise interventions. Appl Physiol Nutr Metab 43:1095–1104

41. Nabkasorn C, Miyai N, Sootmongkol A, Junprasert S, Yamamoto H, Arita M, Miyashita K (2006) Effects of physical exercise on depression, neuroendocrine stress hormones and physiological fitness in adolescent females with depressive symptoms. Eur J Public Health 16:179–184

42. Pedersen BK (2019) Physical activity and muscle-brain crosstalk. Nat Rev Endocrinol 15:383–392

43. Heinemeier K, Langberg H, Kjaer M (2003) Exercise-induced changes in circulating levels of transforming growth factor-beta-1 in humans: methodological considerations. Eur J Appl Physiol 90:171–177

44. Albert U, Brugnoli R, Caraci F, Dellosso B, Di Sciascio G, Tortorella A, Vampini C, Cataldo N, Pegoraro V (2016) Italian psychiatrists' perception on cognitive symptoms in major depressive disorder. Int J Psychiatry Clin Pract 20:2–9

45. Martinsen EW, Hoffart A, Solberg Ø (1989) Comparing aerobic with nonaerobic forms of exercise in the treatment of clinical depression: A randomized trial. Compr Psychiatry 30:324–331

46. Thirlaway K, Benton D (1992) Participation in physical activity and cardiovascular fitness have different effects on mental health and mood. J Psychosom Res 36:657–665

47. Doyne EJ, Ossip-Klein DJ, Bowman ED, Osborn KM, McDougall-Wilson IB, Neimeyer RA (1987) Running Versus Weight Lifting in the Treatment of Depression. J Consult Clin Psychol 55:748–754

48. Dunn AL, Marcus BH, Kampert JB, Garcia ME, Kohl HW, Blair SN (1999) Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: a randomized trial. JAMA 281:327–334