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## **Physical Activity as a Protective Factor Against Depression Incidence and as a Treatment for Depression - a literature review**

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## **Abstract**

### **Introduction:**

Depression is one of the most common and serious mental health disorders that negatively affects how you feel, think, and act. This syndrome is characterized by stress and emotion dysregulation, involving compromised structural integrity of frontal-limbic networks. It causes persistent feelings of sadness and a lack of interest in activities once enjoyed. Effective treatments, including therapy and medication, are available and can help manage the symptoms and improve quality of life. The aspect of physical activity as a component of depression treatment is currently being intensively studied.

## Purpose of work:

This work provides a review of the knowledge on the relationship between physical activity and depression.

## Summary:

Depression has a profound impact on the personal life, relationships, and work of those affected by the condition. Pharmacological and psychological interventions remain the cornerstone of treatment. However, these treatments do not produce the desired effects in all patients. This article presents the conclusion that physical exercise, as an alternative method for preventing and treating depression, is effective. The recent literature also suggests significant mental health benefits from being physically active, even at levels below the public health recommendations. Therefore, health practitioners should encourage any increase in physical activity to enhance mental health.

**Keywords:** Depression; Exercise; Mental health; Non-pharmacological; Review.

## 1. Introduction

Depression is a complex, chronic mental disorder marked by persistent low mood, pessimism, and anhedonia. Other symptoms are a lack of interest in everyday activities, sleep disturbances, an inability to find joy in life, and suicidal thoughts with or without suicidal plans or attempts [1, 2]. Depression is the leading risk factor for suicide [3]. According to the World Health Organization, depression is a leading cause of both mental and physical disability [4]. The global number of new cases has increased by nearly 50% over the past 30 years, now affecting more than 264 million people of all ages [5]. The economic costs in the United States have risen by 48% over the past decade [6]. The primary treatment for individuals with confirmed depression currently involves antidepressants and psychotherapies [7].

Physical activity according to the World Health Organization encompasses any bodily movement produced by skeletal muscles that requires energy expenditure. This includes all forms of movement, whether during leisure time, for transportation, or as part of work. Both moderate- and vigorous-intensity physical activities are beneficial for health.



Figure 1. WHO recommendations for Physical Activity in Adults [8]

## **2. General information about Depression**

### **a. Diagnosis of Depression According to DSM-5**

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), offers comprehensive criteria for diagnosing major depressive disorder (MDD) and related depressive conditions. The DSM-5 categorizes depressive disorders into several types, reflecting a broad spectrum of symptom severity and duration. This chapter outlines the key diagnostic criteria and changes introduced in DSM-5 for diagnosing depression.

MDD is characterized by the presence of one or more major depressive episodes (MDEs). An MDE is defined by the following criteria:

- I. Five or more symptoms present during the same 2-week period:
  - A. Depressed mood most of the day, nearly every day.
  - B. Markedly diminished interest or pleasure in all, or almost all, activities most of the day.
  - C. Significant weight loss when not dieting, weight gain, or decrease or increase in appetite.
  - D. Insomnia or hypersomnia.
  - E. Psychomotor agitation or retardation.
  - F. Fatigue or loss of energy.
  - G. Feelings of worthlessness or excessive or inappropriate guilt.
  - H. Diminished ability to think or concentrate, or indecisiveness.
  - I. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan for committing suicide.
- II. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- III. The episode is not attributable to the physiological effects of a substance or another medical condition.

The DSM-5 excludes MDD diagnosis if the symptoms are better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders. [9]

### **b. Risk factors of Depression**

Several risk factors contribute to the development of depression, including genetic predisposition, adverse life events, chronic medical conditions, and socio-economic challenges. Research indicates that people who have experienced abuse, severe losses, or other significant life stressors are at higher risk of developing depression. Here are some examples of studies.

**Genetic factor:** A study involving 415 older French women investigated the association between GPR50 polymorphisms (a melatonin-related receptor) located on the X-chromosome and the risk of developing depression. The researchers discovered that homozygosity for the minor allele of rs561077 was a significant risk factor for incident depression in these women. However, they did not find a similar risk increase associated with the polymorphisms rs13440581 and rs2072621 [10].

**Sociodemographic characteristics:** Older age was identified as a risk factor for depression in five studies [11-15]. However, other studies did not find a significant association between older age and depression [16-17]. Female gender was associated with a higher incidence of depression in studies [18,19], other studies found no significant association between female gender and depression [11,20]. Lower childhood socioeconomic status was identified as a significant risk factor for depression in one study [21].

**Lifestyle factors:** A physical activity was identified as a protective factor [22,23]. The analysis of “cigarette smoking” produced mixed results in studies. Three studies identified it as a risk factor for depression [11,13,14], while three other studies found no significant association [16,22,24]. Alcohol consumption was found to be insignificant in all five studies analyzing this factor [11,13,16,24,25]. However, a German study identified at-risk drinking as a significant risk factor for depression [18]. Additionally, the COVID-19 pandemic has exacerbated mental health issues globally, leading to an increase in depression diagnoses and a heightened burden on healthcare systems.

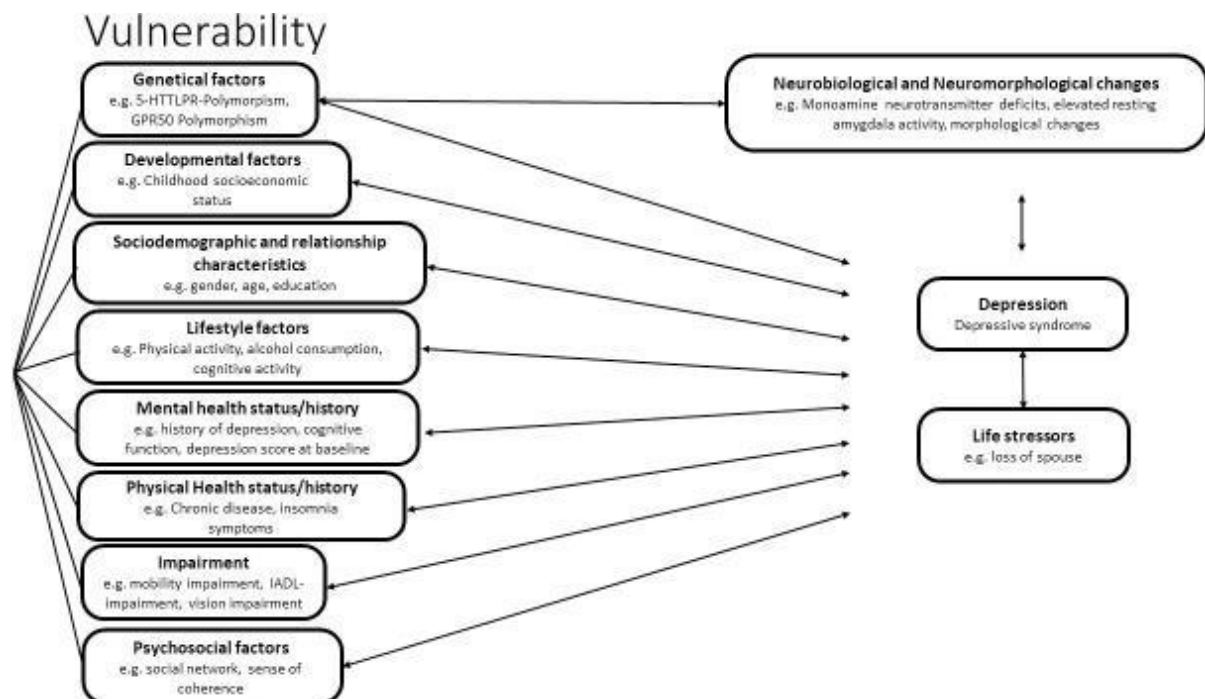


Figure 2. Risk factors for incident depression [26].

### c. Pharmacological treatment of Depression

Pharmacological treatment is a cornerstone in the management of major depressive disorder (MDD), aiming to alleviate symptoms, improve quality of life, and prevent relapse. Antidepressants are the primary class of medications used and are categorized into several groups based on their mechanisms of action. Types of antidepressants: selective serotonin reuptake inhibitors (SSRIs): (fluoxetine, sertraline, citalopram) the first-line treatment due to their favorable side effect profile and efficacy. They work by increasing serotonin levels in the brain, which can help improve mood and emotional stability [27].

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs): (venlafaxine, duloxetine) enhance the levels of both serotonin and norepinephrine, offering another effective treatment option, particularly for patients who do not respond to SSRIs.

Tricyclic Antidepressants (TCAs): (amitriptyline, nortriptyline) are older antidepressants that are effective but often reserved for treatment-resistant depression due to their more pronounced side effects and toxicity in overdose.

Monoamine Oxidase Inhibitors (MAOIs): (phenelzine, tranylcypromine) are another class of older antidepressants. They are effective but typically used less frequently due to dietary restrictions and potential drug interactions.

The choice of antidepressant is influenced by factors such as the patient's previous response to medications, side effect profiles, comorbid conditions, and potential drug interactions. While SSRIs and SNRIs are generally well-tolerated, some patients may experience side effects such as gastrointestinal disturbances, weight gain, or sexual dysfunction [28,29].

#### **d. Psychological therapies of Depression**

Over the past decades, various types of psychotherapy for depression have been developed and tested in primary care settings. Psychotherapy can be defined as “the informed and intentional application of clinical methods and interpersonal stances derived from established psychological principles for the purpose of assisting people to modify their behaviors, cognitions, emotions, and/or other personal characteristics in directions that the participants deem desirable” [30]. Psychological therapies are effective for treating depression in primary care settings, offering longer-lasting effects than pharmacological treatments. These therapies are preferred by most patients and can be flexibly implemented in various formats and tailored to different target groups [31]. Types of therapy used to treat depression include cognitive-behavioral therapy (CBT), behavioral activation therapy (BAT), interpersonal psychotherapy (IPT), problem-solving therapy, non-directive counseling, brief psychodynamic therapies, life review therapy and mindfulness-based CBT [32-35]. Research indicates that the efficacy of various psychotherapy types for depression does not differ significantly. Both direct comparisons of different therapies [36] and network meta-analyses [37] have shown that all major psychotherapeutic approaches yield similar outcomes.

#### **e. Physical Activity as a treatment for Depression**

Given the significant impact of depression on individuals and society, it is crucial to identify modifiable risk factors that can be altered. Increasingly, it is recognized that lifestyle behaviors, such as physical activity (PA) and exercise, play a role in the risk of developing depression. These behaviors can be effective strategies for treating depression, alleviating depressive symptoms, enhancing quality of life, and improving physical health outcomes. Studies across various countries and cultures have consistently shown that higher levels of physical activity are associated with reduced depressive symptoms. For instance, recent findings from the Brazilian National Health Survey, which included 59,399 participants, revealed that lack of leisure-time physical activity was linked to depression. This association was observed in young males, middle-aged individuals, and older adults [38].

Furthermore, a study conducted across 36 countries consistently found that lower levels of physical activity, defined as less than 150 minutes of moderate to vigorous activity per week, were associated with increased rates of depression [39].

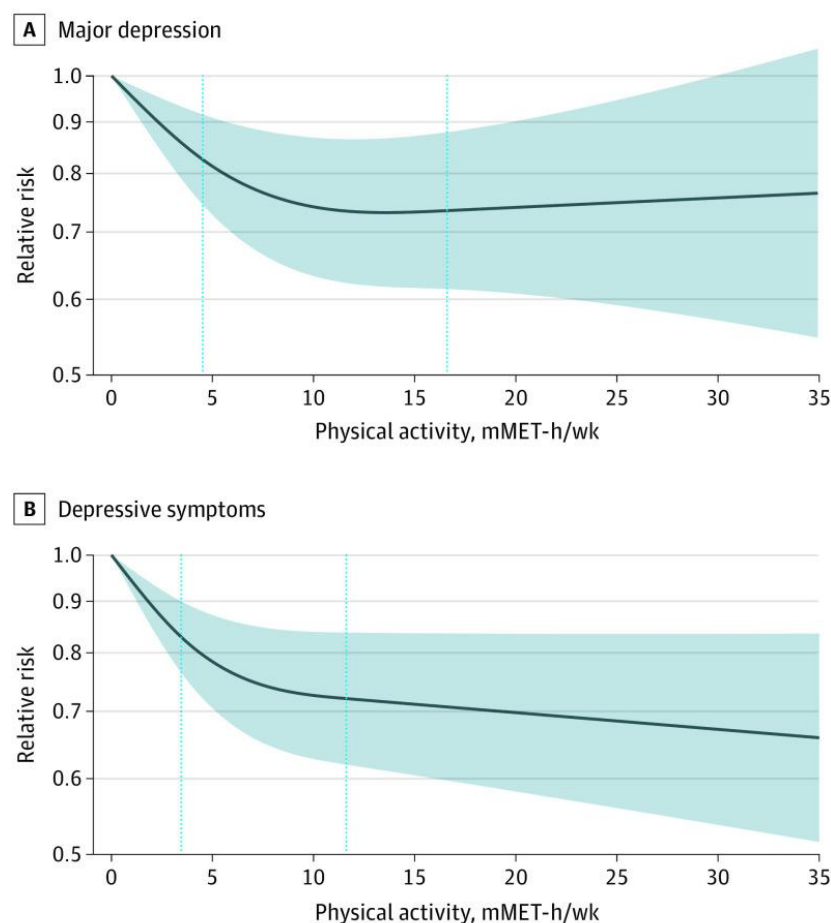


Figure 3. The relationship between physical activity and incidence of Major Depression and Elevated Depressive Symptoms [40].

Physical activity has been shown to influence a range of biological pathways, including inflammatory cytokines, oxidative stress, neurotrophins, and neurogenesis [41, 42]. In animal models, exercise has demonstrated biological effects through multiple mechanisms, such as enhanced neurogenesis [43] and modulate monoamine systems, increasing the expression of 5HT in animal models [44], which is believed to contribute to its antidepressant effects [45]. The chronic effects of regular exercise may help regulate the neuroendocrine axis and normalize cortisol levels [46], while also increasing circulating beta-endorphins [47].

**Conclusion:** This review highlights the strong mental health benefits associated with physical activity, suggesting that engaging in regular exercise can significantly reduce the risk of depression and alleviate symptoms in individuals already suffering from the condition. Biological mechanisms such as enhanced neurogenesis, increased levels of neurotrophic factors, and regulation of the neuroendocrine axis are pivotal in the positive effects of physical activity on mental health. Exercise offers numerous benefits for both physical and mental health and should be encouraged for everyone.

**Disclosure:****Author's contribution:**

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methodology: Anna Szeliga, Agata Szostak, Karolina Korta;  
software: Agata Szostak, Magdalena Graca, Weronika Łowicka;  
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resources: Konrad Wawszkiewicz, Magdalena Graca;  
data curation: Maria Janina Śmigielska-Mikołajczyk, Anna Szeliga;  
writing - rough preparation: Karolina Oluszcak, Liliana Dyląg;  
writing - review and editing: Kinga Szopińska, Weronika Łowicka;  
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project administration: Karolina Oluszcak, Kinga Szopińska

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**Bibliography:**

1. Filatova EV, Shadrina MI, Slominsky PA. Major depression: one brain, one disease, one set of intertwined processes. *Cells*. 2021; 10:1283.
2. R. Cui, Editorial: a systematic review of depression *Curr. Neuropharmacol.*, 13 (4) (2015)
3. Péter Torzsa, Lilla Szeifert, Klaudia Dunai, László Kalabay, Márta Novák, Diagnosis and therapy of depression in family practice, *Orv Hetil.* 2009 Sep 6;150(36):1684-93.



4. Monroe SM, Harkness KL. Major depression and its recurrences: life course matters. *Annu Rev Clin Psychol.* 2022; 18:329–357.
5. Liu Q, He H, Yang J, Feng X, Zhao F, Lyu J. 2020. Changes in the global burden of depression from 1990 to 2017: findings from the Global Burden of Disease study. *J. Psychiatr. Res.* 126:134–40
6. Greenberg PE, Fournier A-A, Sisitsky T, Simes M, Berman R et al. 2021. The economic burden of adults with major depressive disorder in the United States (2010 and 2018). *Pharmacoeconomics* 39:653–65
7. Schuch, Felipe Barreto PhD; Stubbs, Brendon PhD, The Role of Exercise in Preventing and Treating Depression, *Current Sports Medicine Reports* 18(8):p 299-304, August 2019.
8. World Health Organization. (2020). WHO guidelines on physical activity and sedentary behaviour: at a glance. World Health Organization. License: CC BY-NC-SA 3.0 IGO
9. American Psychiatric Association, ed. (2022). *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR)*. Washington, DC, USA: American Psychiatric Publishing. ISBN 978-0-89042-575-6.
10. Ryan J, Carrière I, Ritchie K et al. (2015) Involvement of GPR50 polymorphisms in depression: independent replication in a prospective elderly cohort. *Brain Behav* 5:e00313.
11. Weyerer S, Eifflaender-Gorfer S, Wiese B et al. (2013) Incidence and predictors of depression in non-demented primary care attenders aged 75 years and older: results from a 3-year follow-up study. *Age Ageing* 42:173–180.
12. Lampinen P, Heikkinen E (2003) Reduced mobility and physical activity as predictors of depressive symptoms among community-dwelling older adults: an eight-year follow-up study. *Aging Clin Exp Res* 15:205–211.
13. Chou K-L (2007) Combined effect of vision and hearing impairment on depression in older adults: Evidence from the English Longitudinal Study of the Ageing. *J Affect Disord*:191–196
14. Chou K-L (2007) Reciprocal relationship between pain and depression in older adults: evidence from the English Longitudinal Study of Ageing. *J Affect Disord* 102:115–123.
15. Conde-Sala JL, Garre-Olmo J, Calvó-Perxas L et al. (2019) Course of depressive symptoms and associated factors in people aged 65+ in Europe: A two-year follow-up. *J Affect Disord* 245:440–450.
16. Makizako H, Shimada H, Doi T et al. (2015) Physical frailty predicts incident depressive symptoms in elderly people: prospective findings from the Obu Study of Health Promotion for the Elderly. *J Am Med Dir Assoc* 16:194–199.
17. Lyness JM, Yu Q, Tang W et al. (2009) Risks for depression onset in primary care elderly patients: potential targets for preventive interventions. *Am J Psychiatry* 166:1375–1383.
18. Lupp M, Luck T, König H-H et al. (2012) Natural course of depressive symptoms in late life. An 8-year population-based prospective study. *J Affect Disord* 142:166–171.
19. Yokoyama E, Kaneita Y, Saito Y et al. (2010) Association between depression and insomnia subtypes: a longitudinal study on the elderly in Japan. *Sleep* 33:1693–1702.

20. Mossaheb N, Weissgram S, Zehetmayer S et al. (2009) Late-onset depression in elderly subjects from the Vienna Transdanube Aging (VITA) study. *J Clin Psychiatry* 70:500–508.
21. Tani Y, Fujiwara T, Kondo N et al. (2016) Childhood Socioeconomic Status and Onset of Depression among Japanese Older Adults: The JAGES Prospective Cohort Study. *The American Journal of Geriatric Psychiatry* 24:717–726.
22. Dong Y, Yang FM (2019) Insomnia symptoms predict both future hypertension and depression. *Preventive Medicine* 123:41–47.
23. Uemura K, Makizako H, Lee S et al. (2018) Behavioral protective factors of increased depressive symptoms in community-dwelling older adults: A prospective cohort study. *Int J Geriatr Psychiatry* 33:e234–e241.
24. Tsutsumimoto K, Makizako H, Doi T et al. (2017) Prospective associations between sedentary behaviour and incident depressive symptoms in older people: a 15-month longitudinal cohort study. *Int J Geriatr Psychiatry* 32:193–200.
25. Dong Y, Yang FM (2019) Insomnia symptoms predict both future hypertension and depression. *Preventive Medicine* 123:41–47.
26. Alexander Maier, Steffi G. Riedel-Heller, Alexander Pabst, Melanie Lupp, Risk factors and protective factors of depression in older people 65+. A systematic review, *Plos One* May 13, 2021
27. Ferguson, J. M. (2001). "SSRI Antidepressant Medications: Adverse Effects and Tolerability." *Primary Care Companion to The Journal of Clinical Psychiatry*, 3(1), 22–27.
28. Cipriani, A., et al. (2018). "Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis." *The Lancet*, 391(10128), 1357–1366.
29. Anderson, I. M. (2000). "Selective serotonin reuptake inhibitors versus tricyclic antidepressants: a meta-analysis of efficacy and tolerability." *Journal of Affective Disorders*, 58(1), 19–36.
30. Campbell LF, Norcross JC, Vasquez MJ, Kaslow NJ. Recognition of psychotherapy effectiveness: the APA resolution. *Psychother.* 2013;50:98.
31. Pim Cuijpers, Soledad Quero, Christopher Dowrick, Bruce Arroll, *Curr Psychiatry Rep.* 2019; 21(12): 129. Published online 2019 Nov 23.
32. Linde K, Sigtermann K, Kriston L, Rucker G, Jamil S, Meissner K, et al. Effectiveness of psychological treatments for depressive disorders in primary care: systematic review and meta-analysis. *Ann Fam Med.* 2015;13:56–68.
33. Ekers D, Webster L, Van Straten A, Cuijpers P, Richards D, Gilbody S. Behavioural activation for depression; an update of meta-analysis of effectiveness and sub group analysis. *Plos One.* 2014;9(6):e100100.
34. Cuijpers P, Donker T, Weissman MM, Ravitz P, Cristea IA. Interpersonal psychotherapy for mental health problems: a comprehensive meta-analysis. *American Journal of Psychiatry.* 2016;173:680–687.
35. Swathi Gujral, Howard Aizenstein, Charles F Reynolds 3rd, Meryl A Butters, Kirk I Erickson, Exercise effects on depression: Possible neural mechanisms, 2017 Nov;49:2–10

36. Cuijpers P, van Straten A, Andersson G, van Oppen P. Psychotherapy for depression in adults: a meta-analysis of comparative outcome studies. *J Consult Clin Psychol.* 2008;76:909–922.
37. Barth J, Munder T, Gerger H, Nuesch E, Trelle S, Znoj H, et al. Comparative efficacy of seven psychotherapeutic interventions for depressed patients: a network meta-analysis. *Plos Med.* 2013;10:e1001454.
38. de Oliveira GD, Oancea SC, Nucci LB, et al. The association between physical activity and depression among individuals residing in Brazil. *Soc. Psychiatry Psychiatr. Epidemiol.* 2018; 53:373–83.
39. Stubbs B, Koyanagi A, Schuch FB, et al. Physical activity and depression: a large cross-sectional, population-based study across 36 low- and middle-income countries. *Acta Psychiatr. Scand.* 2016; 134:546–56.
40. Pearce M, Garcia L, Abbas A, Strain T, Schuch FB, Golubic R, Kelly P, Khan S, Utukuri M, Laird Y, Mok A, Smith A, Tainio M, Brage S, Woodcock J. Association Between Physical Activity and Risk of Depression: A Systematic Review and Meta-analysis. *JAMA Psychiatry.* 2022 Jun 1;79(6):550-559. doi: 10.1001/jamapsychiatry.2022.0609. PMID: 35416941;
41. Berk M, Kapczinski F, Andreazza AC, Dean OM, Giorlando F, Maes M, Yucel M, Gama CS, Dodd S, Dean B, Magalhães PV, Amminger P, McGorry P, Malhi GS: Pathways underlying neuroprogression in bipolar disorder: focus on inflammation, oxidative stress and neurotrophic factors. *Neurosci Biobehav Rev.* 2010, 35 (3): 804-817.
42. Berk M, Conus P, Kapczinski F, Andreazza AC, Yucel M, Wood SJ, Pantelis C, Malhi GS, Dodd S, Bechdolf A, Amminger GP, Hickie IB, McGorry PD: From neuroprogression to neuroprotection: implications for clinical care. *Med J Aust.* 2010, 193 (4 Suppl): S36-S40.
43. Ernst C, Olson AK, Pinel JPJ, Lam RW, Christie BR: Antidepressant effects of exercise: evidence for an adult-neurogenesis hypothesis?. *J Psychiatry Neurosci.* 2006, 31 (2): 84-92.
44. Dey S, Singh RH, Dey PK: Exercise training: significance of regional alterations in serotonin metabolism of rat brain in relation to antidepressant effect of exercise. *Physiol Behav.* 1992, 52 (6): 1095-1099. 10.1016/0031-9384(92)90465-E.
45. Chaouloff F: Effects of acute physical exercise on central serotonergic systems. *Med Sci Sports Exerc.* 1997, 29 (1): 58-62. 10.1097/00005768-199701000-00009.
46. Mastorakos G, Pavlatou M, Diamanti-Kandarakis E, Chrousos GP: Exercise and the stress system. *Hormones (Athens).* 2005, 4 (2): 73-89.
47. T B, G N, I B, Tefner I, Kádas E, Géher P: The effect of physical therapy on beta-endorphin levels. *Eur J Appl Physiol.* 2007, 100 (4): 371-382. 10.1007/s00421-007-0469-9. Epub 2007 May 5