

A Critical Review of Aerobic Exercise and Depressive Symptoms in People with Major Depressive Disorder

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Abstract

Depression is a prevalent mental disorder worldwide, with significant implications for individuals' well-being and societal burden. The use of antidepressants and cognitive behavioural therapy (CBT) are common treatment approaches. Alternative treatments with fewer side effects and lower costs are needed. This review explores the biological and psychological mechanisms underlying the relationship between exercise and depression, including neuroplasticity, neuroendocrine function, inflammation, self-esteem, and self-efficacy. Five selected studies, meeting specific inclusion criteria, were analysed, with three studies demonstrating a significant positive effect of aerobic exercise on reducing depressive symptoms in MDD. One study showed no significant difference, possibly due to participant dropout and confounding factors. Some similarities in exercise duration, intensity and frequency are also found between current guidelines and the findings. In conclusion, although evidence suggests a positive effect of aerobic exercise on depressive symptoms in MDD, further research with rigorous methodology is needed to establish optimal exercise parameters for this population.

Keywords

Scoping review, aerobic exercise, depression, major depressive disorder.

1. Background

Depression is a common worldwide mental disorder. It is estimated that 280 million people (3.8%) were affected by depressive disorder worldwide (World Health Organization, 2021). While in the US, 8.4% of adults (21 million) had at least one episode of major depressive disorder (MDD), and the prevalence (17%) was found to be highest among young adults aged 18-25 (SAMHSA, 2021). The situation worsened during the COVID-19 pandemic. In comparison with before the pandemic, more than twofold number of people were affected by depressive symptoms during the pandemic (Ettman et al., 2020). People's ability to work and interpersonal relationships can be impacted by depression, and at worst, it can cause suicide (WHO, 2021). Depression is also associated with other medical conditions, such as alcohol addiction, type 2 diabetes, etc (Biddle et al., 2021). In 2004, depression became the third leading burden of disease in disability-adjusted life years, and it was predicted to become the first burden of disease in 2030 (WHO, 2008).

Currently, antidepressants are the first line of treatment for depression (Biddle et al., 2021). Since 1999-2002, the use of antidepressants in the last month in individuals over 12 years old has significantly increased from 7.7% to 12.7% in 2011-2014 (Pratt et al., 2017). Cognitive behaviour therapy (CBT) which requires an interview with therapists is another popular treatment for depression (Wenzel & Amy, 2016). However, due to the side effects of antidepressants and the high cost of CBT, alternative treatment with fewer side effects and lower costs is needed. In a systematic review and meta-analysis, Cooney et al. (2013) indicated that exercise has a moderate clinical effect on depression, and its effect might be similar to that of pharmacological treatment. But the forms of exercise that the researchers covered in the

study varied. Furthermore, De Souza Moura et al. (2015) conducted a systematic review of the studies before 2015 to investigate the difference between aerobic and non-aerobic exercise in people with depression. In the five selected studies reviewed, only one study indicated a significant positive effect of aerobic and non-aerobic exercise on depression, while the other four studies reported no significant effect of both aerobic and non-aerobic exercise. But some benefits of aerobic exercise were identified by the aerobic exercise group, such as an increase in maximal oxygen uptake and a reduction of waist perimeter (De Souza Moura et al., 2015).

Based on the above, this essay aims to investigate whether aerobic exercise has an effect on reducing depressive symptoms in people with major depressive disorder (MDD) by critically reviewing papers published after 2014. Furthermore, how this evidence relates to current exercise guidelines for people with MDD will be discussed.

2. Mechanism

Exercise can impact a variety of biological and psychological processes of an individual, and it may implicate the pathophysiology of depression (Kandola et al., 2019). Potential mechanisms that exercise can improve depression can be explained through neuroplasticity, neuroendocrine, inflammation and psychological factors (e.g., self-esteem and self-efficacy) (Kandola et al., 2019). One popular hypothesis in neuroplasticity is that MDD is associated with the decrease in hippocampal volume, and exercise works as an antidepressant that can increase the synthesis of hippocampal neurons (Durstine et al., 2016). In a meta-analysis, brain magnetic resonance images from 1728 MDD patients and 7199 healthy people were analysed by Schemaal et al., (2016) who indicated that significantly lower hippocampal volumes were found in patients with MDD compared to healthy participants. Videbech et al. (2004) also found that hippocampal volume decreased on both the left and right sides of the brain in the patients by comparing with healthy participants. However, exercise can improve the hippocampal volume. In a meta-analysis that included 22 studies, Wilckens et al. (2021) demonstrate that over 24 weeks of moderate-intensity exercise has an effect on increasing hippocampal volume. Additionally, aerobic exercise was also found to improve left hippocampal volume in a meta-analysis extracting 14 studies with 737 patients (Firth et al., 2018).

Potential mechanisms of exercise improving depression can also be explained by psychological processes. In a systematic review, Keane & Lisa (2017) demonstrated that young people with low self-esteem are associated with comorbidity of depression. Nguyen et al. (2019) also indicate that low self-esteem is associated with depression, which can impact people's quality of life and suicidal ideation. What is worse, the relationship between self-esteem and depression can be cyclical (Kandola et al., 2019), which means low self-esteem can lead to depression and further exacerbate self-esteem. However, exercise might break this circle. An umbrella review concludes that physical activity positively improves mental health and physical self-concept, a component of self-esteem (Dale et al., 2019). A similar result has also been reported in a study with a quasi-experimental design. Rao et al. (2020) demonstrate that improvement in self-esteem and quality of life was found in the intervention group of aerobic exercise. In addition, low self-efficacy is another psychological factor related to depression. A longitudinal cohort study indicates that a low level of self-efficacy is associated with a greater risk of depressive symptoms (Taneichi et al., 2013). In a study with a quasi-experimental design, significant improvement in self-efficacy was found in the aerobic exercise programme, compared with the control group (CG) (Odunaiya et al., 2022).

3. Discussion

3.1. Evidence of aerobic exercise

In this session, whether aerobic exercise has an effect on improving depressive symptoms will be discussed by five selected papers. These papers were included according to the following criteria: 1) Study is designed in randomised control trial; 2) All the participants were diagnosed with MDD; 3) Only usual therapy was conducted in the CG; 4) aerobic exercise was conducted in the intervention group; 5) The outcome of the studies was measured by a rating scale of depression. A summary of the five selected papers is presented in Table 1.

Three Randomised control trials (RCT) report a positive effect with a large effect size from aerobic exercise in reducing depressive symptoms (Legrand & Neff, 2016; Moraes et al., 2020; Wunram et al., 2018). In the study conducted by Legrand & Neff (2016), the duration of the intervention only lasted 10 days but the stretching exercise was conducted as a placebo group to compare with the intervention and control group, which enhance the quality of the study. The researchers indicate a significant large effect in the intervention group (Cohen's $d = -1.06$; $p = 0.012$) by comparing with the CG, and no significant difference was reported between the placebo group and intervention group. A similar effect size was also found in a semi-RCT by Wunram et al. (2018). No significant effect was found after the 6-week intervention and further 8-week follow-up, but in 26 weeks, compared with the CG, a statistically significant effect was reported in the aerobic exercise group (Cohen's $d = 0.85$; $p = 0.037$). And the remission rate is 71.4% in the aerobic exercise group, with 25% in the CG. In contrast, a larger effect size was reported in the study conducted by Moraes et al., (2020). By comparing strength training, aerobic training and CG, the largest effect size was found in the aerobic training group ($E_s = 2.8$; $p = 0.003$), with a smaller effect size in the strength training group ($E_s = 1.5$; $p = 0.001$) (Moraes et al., 2020). In addition, a positive effect was also reported in a study conducted by Schuch et al. (2015). Researchers indicate that after 2 weeks of intervention, there is a significant difference in the scores of HAM-D, with 4.41 points (95%CI: 7.57-1.25; $p = 0.007$) by comparing with the CG.

However, a study indicates no difference in reducing depressive symptoms between the aerobic exercise group and the control group (Kruisdijk et al., 2019). Among these five studies, Kruisdijk et al. (2019) conducted the longest intervention with aerobic exercise twice a week for 6 months. Compared with the CG, although a large effect size was found in secondary outcomes (e.g. aerobic capacity and BMI) and scores on HAM-D17 both decreased in the two groups, no significant difference in reducing depressive symptoms was found (Cohen's $d < 0.2$; $p = 0.73$) between groups. Some issues in the study might induce this result. The response rate is very low in the study, with 73.8% of the participants excluded at the beginning and a 55% drop-off rate at 6 months. Additionally, as reported in the study, the participants in the control group were allowed to do low-intensity exercise (walking and recreational sports). This can become a confounder which might reduce the difference in the effect between the intervention and control group.

Based on the above, it is believed that aerobic exercise has a positive effect on improving depressive symptoms for people with MDD, but the magnitude of the effect differs in these studies. This might be because of the different intensities, frequencies, durations and types of the aerobic exercise program in the study. In the three studies with a large effect size (Legrand & Neff, 2016; Moraes et al., 2020; Wunram et al., 2018), 65–75% of the maximal heart rate, 60% of the VO₂ max and an average of 60-70% maximal wattage in spiroergometry were reported, which refers to the criteria of moderate-to-vigorous exercise. Although the aerobic exercise program only processed 10 days in the study from Legrand & Neff (2016), the 10-day intervention is continuous with no more than two days break. However, no specific intensity of exercise was required for the participants in the study conducted by Schuch et al. (2015). The

intervention only required a total volume of exercise of 16.5 kcal/kg of weight/week, and the aerobic exercise program only lasted three times per week for 2 weeks. Thus, further high-quality study to investigate the dose-response effect of aerobic exercise in reducing depression is warranted.

Furthermore, some limitations were identified. 1) Due to the nature of the intervention, it is impossible to blind the patients or researchers in the study. This might raise the participant's motivation in the CG, which can diminish the potential difference between the intervention and control group (Biddle et al., 2021). 2) Only two studies (Kruisdijk et al., 2019; Moraes et al., 2020) report the allocation concealment, while others do not report or the concealment is unclear. This can increase selection bias in the study.

3.2. Exercise recommendation for people with depression

According to the guideline of management for children and young people with depression by the National Institute for Health and Care Excellence, exercise is suggested to maintain people's mental health. A moderate duration (45 minutes to 1 hour) exercise program of 3 times per week for 10-12 weeks under supervision is suggested to be considered (NICE, 2019). Although no intensity or type of exercise was mentioned in the guideline, the duration (45 mins to 1 hour) is similar to the exercise program of the five studies after adding warm-up and cool-down or stretching part in each session.

In the Recommendations for Physical Activity or Exercise in Chronic Conditions, it is suggested that high-functioning patients with depression and no further comorbid conditions should follow the exercise guidelines provided by the ACSM (Durstine et al., 2016). A specific aerobic exercise program is included for exercise prescription in the ACSM guideline. This aligns with the findings discussed in the five papers, suggesting that aerobic exercise has a positive effect on improving depressive symptoms for patients with MDD. It is recommended that 30-60 minutes of moderate-to-vigorous exercise 3-5 times per week can maintain health/fitness benefits (ACSM, 2018). This duration and intensity are similar to the exercise program in the five studies, but only two studies (Legrand & Neff, 2016; Schuch et al., 2015) match the frequency recommendation from the ACSM guideline. Regarding the total volume of exercise, only one study from (Schuch et al., 2015) refers to a requirement of the total volume of exercise (16.5 kcal/kg of weight/week), which is similar to the recommendation of 1,000 kcal/week. But the evidence of the dose-response effect of exercise in reducing depression is still limited (US PAGAC, 2018).

4. Conclusion

Although the specific pathophysiology of aerobic exercise in improving depression is still unclear, some potential mechanisms of aerobic exercise improving depressive symptoms have been explained by neuroplasticity and psychology in this essay. By discussing five recent related papers, it is believed that aerobic exercise has a positive effect in improving depressive symptoms for people with MDD. It seems that there is a large effect size in aerobic exercise, but due to the biases and limitations of the studies, the evidence supporting this conclusion is still inadequate. Exercise is recommended in the NICE guideline for management of depression and aerobic exercise is included in the exercise prescription from the ACSM guideline. But the dose-repose effect of exercise on depression is still limited, further high-quality studies are warranted.

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Table 1 Summary of the five papers by design, participants, intervention, main finding and study quality

Study	Method		Participants		Intervention		Main findings	Study quality	
	Design	Outcome measure	No	Type	Aerobic exercise type (intensity)	duration		Allocation concealment	Blinded
Kruisdijk et al., (2019)	RCT	HAM-D17	46	Patients with MDD were recruited from three specialised mental health care institutions	1. Intervention: 30 mins Nordic walking or running, twice a week (at least 60% of maximum heart rate) 2. low-intensity exercise is allowed in the control group	6 months	In comparison with the control group, large effects were reported in aerobic capacity and BMI in the intervention group. No difference was found between the	Yes	No

							intervention and control group, but scores on the HAM-D17 decreased in both groups.		
Legrand & Neff, (2016)	RCT	BDI-II	35	Patients diagnosed with MDD, with antidepressant drug therapy less than two weeks	1. 30 mins outdoor brisk walking or jogging every day (65–75% of maximal heart rate). 2. Stretching exercise (placebo group).	10 days	In comparison with the control group, a large effect size (Cohen's $d=-1.06$) was reported in the aerobic exercise group, and the data is statistically significant ($p=0.012$). No significant difference was found in the placebo group.	Unknown	No
Moraes et al., (2020)	RCT	HAM-D	27	The patients with MDD were selected from the Institute of Psychiatry	20 mins exercise on stationary bikes or treadmills, twice a week (60% of the VO2 max)	12 weeks	In comparison with the control group, a large effect size ($Es=2.8$, $p=0.003$) was reported in the aerobic exercise group.	Yes	No
Wunram et al., (2018)	Semi-RCT	DIKJ	43	Patients with MDD were recruited from the Department of Psychiatry at a university	30 mins stationary cycles (average 60-70% maximal wattage in spiroergometry), three times a week	6 weeks	No significant effect was found after 6 weeks of intervention and 14 weeks of follow-up. But at 26 weeks follow-up, in comparison with the control group, a statistically significant result was found in the aerobic group ($F=3.0$, $df=39.1$, Cohen's $d=0.85$, $p=0.037$).	Unknown	No
Schuch et al., (2015)	RCT	HAM-D	25	Patients diagnosed with MDD by the Mini International Neuropsychiatric Interview were recruited in the study.	Power bike or treadmill or "transport" machine, three times a week (flexible intensity, a dose of 16.5 kcal/kg of weight/week of aerobic exercise)	2 weeks	In comparison with the control group, the score on depression was lower in the intervention group, with a significant difference of 4.41 points (95%CI:7.57-1.25; $p=0.007$) in the second week. But no difference in remission was found between groups.	Unknown	No

Beck Depression Inventory (BDI-II); Body Mass Index (BMI); Major Depressive Disorder (MDD); Hamilton Depression Rating Scale (HAM-D); Depressions Inventar für Kinder und Jugendliche (DIKJ); Randomised control trial (RCT)