REVIEW ARTICLE

Effects of exercise and physical activity on depression

P. C. Dinas · Y. Koutedakis · A. D. Flouris

Abstract

Introduction Depression is a very prevalent mental disorder affecting 340 million people globally and is projected to become the leading cause of disability and the second leading contributor to the global burden of disease by the year 2020. *Aim* In this paper, we review the evidence published to date in order to determine whether exercise and physical activity can be used as therapeutic means for acute and chronic depression. Topics covered include the definition, classification criteria and treatment of depression, the link between β-endorphin and exercise, the efficacy of exercise and physical activity as treatments for depression, properties of exercise stimuli used in intervention programs, as well as the efficacy of exercise and physical activity for treating depression in diseased individuals. *Conclusions* The presented evidence suggests that exercise and physical activity have beneficial effects on depression symptoms that are comparable to those of antidepressant treatments.

Keywords Exercise · Depression · Physical activity · Mood · β-Endorphin

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Introduction

Depression is a very prevalent mental disorder affecting 340 million people globally—independently of age, sex, and ethnic background—and is projected to become the leading cause of disability and the second leading contributor to the global burden of disease by the year 2020 [1, 2]. Current evidence also shows that 9% of children by age 14 have already experienced at least one episode of severe depression [3], while up to 10% of adolescents are affected by a major depressive disorder [4]. These statistics are a consequence of the multi-faceted effects of depression on health and well-being [1]. Indeed, individuals suffering from depression show low levels of mood, lack of interest or pleasure, disrupted appetite or sleep, low self-worth, feelings of guilt, deprived concentration and lack of energy. Very often these problems become chronic and lead to disability or, even worse to suicide attempts [1].

Recent reports conclude that depression can be reliably diagnosed in primary care and can be treated through pharmacological agents and psychotherapy with a 60–80% success [5]. However, only 10–25% of those affected by depression receive treatment for their condition, either due to lack of resources and/or trained providers or the social stigma associated with this condition [1, 5]. Therefore, it is very important to discover alternative therapeutic methods for depression. In this light, encouraging evidence has shown that exercise and physical activity have beneficial effects on depression symptoms that are often comparable to those of antidepressant treatments [6, 7]. Yet, to our knowledge, these new evidence linking exercise and physical activity with depression have not been critically evaluated. Therefore, in this paper, we review the evidence published to date in order to determine whether exercise and physical activity can be used as therapeutic means for

acute and chronic depression. It is hoped that the information provided will be valuable not only to physicians, exercise psychologists and physiologists, but also to those interested in personal or public health, politics and economics.

Approach

A comprehensive search in PubMed and Science Direct was conducted using MeSH terms that are germane to acute and chronic depression (e.g., depression symptoms, mood, depressive disorder, psychotherapy) in conjunction with exercise and psychophysical mechanisms (e.g., exercise, physical activity, β-endorphin, opioids, serotonin, pituitary gland). The search also included the articles cited in the identified papers. All articles resulting from the above methods were considered in this review, and only those deemed irrelevant (i.e., not directly studying the effects of exercise and physical activity on depression) were omitted. The following pages cover information regarding exercise and physical activity as treatments for depression, the endorphin hypothesis and the hormonal effects of β-endorphins on depression, the effects and the required frequency and mode of exercise and physical activity on depression, as well as the influence of an individual's age on the successfulness of exercise and physical activity interventions for depression.

## Definition, classification criteria and treatment of depression

Depression represents a major illness with both health and social consequences similar to chronic diseases such as diabetes, congestive heart failure and hypertension [5]. According to the World Health Organization, depression is an illness characterized by negative mood, decreased interest for pleasure, feelings of guilt, uneasy sleep, decreased appetite and energy, as well as poor brain concentration [1, 2]. These feelings can be either acute or chronic, resulting in a reduced interest for life which can lead to extreme actions such as suicide [2]. The criteria based on which classification of depression is accomplished are appointed by the International Classification of Diseases (ICD-10) for worldwide use [8] and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) developed in the United States [9]. Generally, these standardized criteria are used to separate "normal" depressed mood caused, for instance, by disappointment, from depressive disorders also known as "affective disorders" and "mood disorders" [8, 9].

Depression is normally treated with various pharmaceutical agents or psychotherapeutic interventions or a combination of these. Current evidence shows that patients seeing a primary care provider are more likely to have a failed treatment than patients seeing a psychiatrist [10]. This, however, does not suggest that pharmacological agents are unsuccessful in the treatment of depression. Indeed, a large number of studies show that different pharmacological treatments are successful in treating acute depressive episodes [5]. In this light, a successful cooperation between primary and specialty mental health sectors is crucial, since most patients with depression first seek help in primary care [11–13]. Therefore, consultative roles for mental health specialists have been recommended in some countries to support primary care physicians in the treatment of depression [14, 15]. Relatively, recent evidence suggests that an exercise science specialist may also need to complement the primary care physicians and mental health specialists in order to successfully tackle depression symptoms and episodes [5]. For instance, it is widely accepted that mood states are highly depended on endorphin secretion [16]. Moreover, according to the endorphins hypothesis, exercise augments endorphin secretion which, in turn, reduces anxiety and depression levels [17]. These notions are further discussed in the following section.

β-Endorphin and exercise

Endorphins are endogenous opioid polypeptide compounds produced by the pituitary gland and the hypothalamus in vertebrates during strenuous exercise, excitement, pain, and they resemble the opiates in their abilities to produce analgesia and a sense of well-being [16]. The opioid system plays a key role in mediating analgesia and social attachment and may also affect depression given the link between β-endorphins and depression symptoms [18–20]. To date, β-endorphin secretion has been used for the diagnosis of depression and it could be used as an agent in a therapeutic strategy [21]. Moreover, available data have shown that the μ-opioidergic system is considerably involved in the etiology of mental disorders, thus providing a rationale for the use of μ-opioid ligands such as β-endorphin in behavioral therapies [16]. A recent meta-analysis concluded that the mechanisms by which exercise may improve depression remain uncertain mainly due to methodological limitations of existing research [22]. Yet, based on recent biological evidence linking the opioid system with mood and depression [16, 19, 23], it seems reasonable to explore a relevant hypothesis that has received considerable attention. According to the 'endorphins hypothesis', exercise augments the secretion of endogenous opioid peptides in

Fig. 1 The endorphins hypothesis mechanism
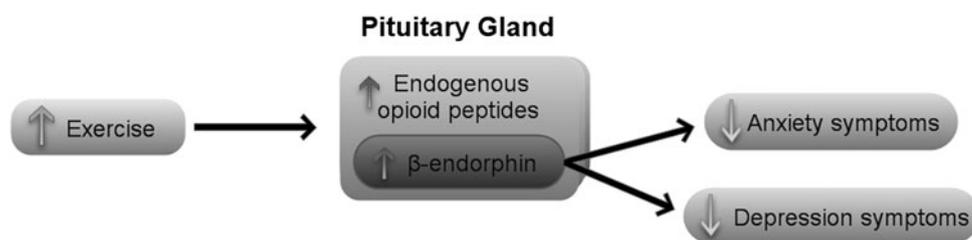
the brain reducing pain and causing general euphoria (Fig. 1) [17, 24, 25]. In turn, the latter reduces anxiety and depression levels [17, 24]. These notions were confirmed by a recent study showing an exercise-induced beneficial effect of endorphins in mood, which suggests that further research is warranted on the endorphins hypothesis [25].

A recent study investigated the endorphins hypothesis in competitive long distance athletes (i.e., training > 4 h per week in the last 2 years) [26]. The participants underwent positron emission tomography "ligand activation" [27], toxicological examinations, and completed the visual analog mood scales [28] at rest and after 2 h of endurance running. Based on a large effect size, the results confirmed the endorphins hypothesis demonstrating that exercise leads to an increased secretion of endorphins which, in turn, improved mood states [26].

β-Endorphin, an endogenous μ-opioid receptor-selective ligand [29], has received much attention in the literature linking endorphins and depression or mood states. β-Endorphin is primarily synthesized in the anterior pituitary gland and cleaved from pro-opiomelanocortin, its larger precursor molecule [30]. It reaches the circulation either through secretion from the pituitary gland or via projection into specific brain regions through nerve fibers [30]. To date, clinical studies have shown an increased level of β-endorphin and μ-opioid receptors in plasma and brain of patients suffering from depression and schizophrenia [31–35]. Moreover, clinical trials on patients with different types of psychiatric disorders (i.e., depression, schizophrenia and neuroses) demonstrated an antidepressant effect of β-endorphin [36]. These results support, in part, the endorphins hypothesis given that exercise of sufficient intensity and duration can increase circulating β-endorphin levels [30, 37]. Indeed, β-endorphin levels of women with cardiologic problems (syndrome of prolapsed of maternal valve) show an increase following an exercise session to a degree that constitutes treatment [38]. Moreover, a recent study demonstrated that exercise and physical activity increased β-endorphin levels in plasma with positive effects on mood [39]. Interestingly, the researchers reported that, independently of sex and age, dynamic and anaerobic exercises increased β-endorphin, while resistance and aerobic exercises seem to have only small effects on β-endorphins [39]. In general, the evidence thus far

suggests that exercise-induced β-endorphin adaptations are depended on the type of exercise and population tested, and may differ in individuals with health problems. Furthermore, some of the proposed mechanisms inducing the exercise-induced β-endorphin changes include analgesia, lactate or base excess, and metabolic factors [30, 37]. Nevertheless, the social element of exercise and its effects on β-endorphin levels has not been examined. While individualized and group-based interventions appear to be equally beneficial for treating depression [40], we remain naïve as to the effects of these protocols on β-endorphin levels.

Exercise, physical activity and depression

It is known for some time that physical activity and exercise are inversely associated with depression levels. A relevant classic study was conducted by Paffenbarger and colleagues [41] who examined questionnaires of 31,000 Harvard College graduates in 1962, 1966, 1977, and 1988. Results showed that physically active individuals reported lower depression levels than their physically inactive peers. These results are supported by a more recent study that examined 5,877 individuals aged 15–54 years showing that physically active individuals report lower levels of depression than non-active individuals [42]. Moreover, there was an inverse linear relationship between physical activity participation and depression with individuals reporting as frequently active showing lower levels of depression, individuals reporting as occasionally active showing higher levels of depression and, finally, individuals reporting as inactive showing the highest levels of depression [42].

The beneficial effects of physical activity and exercise on depression symptoms and general mood have been confirmed in individuals of all ages. In children and adolescents, a small beneficial effect of exercise in reducing depression and anxiety scores has been recorded, yet the small number of studies included and the clinical diversity of participants, interventions and methods of measurement limit the ability to draw conclusions [43]. In younger adults, a previous investigation examined whether daily activity and the tendency to participate in exercise are

associated with mood states in a student cohort [44]. The results showed that mood tends to be higher in a day an individual exercises as well as that daily activity and exercise overall are strongly linked with mood states. In line with these findings, a recent study showed that exercise significantly improves mood states in non-exercisers, recreational exercisers, as well as marathon runners [45]. More importantly, the effects of exercise on mood were twofold in recreational exercisers and marathon runners [45].

In older adults, exercise interventions have shown very promising results for alleviating symptoms of major depression [46]. These findings are supported by a more recent study examining the effects of physical activity in a sample of depressed elderly patients showing that physical activity is associated with reduced concurrent depression [47]. Based on these findings, it was suggested that physical activity may be especially helpful in the context of medical problems and major life stressors, while encouraging depressed elderly patients to engage in physical activity is likely to have potential benefits on clinical depression symptoms [47]. Finally, elderly who remain physically active across time demonstrate lower levels of depression symptoms compared to those who adopt inactive lifestyles when they get older [48].

Exercise and physical activity as treatments for depression

A recent meta-analysis reported a large clinical effect of physical activity and exercise interventions on the symptoms of depression for adults of both sexes [22]. More specifically, aerobic exercise indicated a moderate clinical effect, while mixed and resistance exercise indicated large effect sizes. Moreover, when compared against other established treatments (i.e., cognitive behavior therapy and antidepressants), exercise appears to produce the same results [22]. Indeed, published evidence shows that exercise and physical activity interventions are generally successful in reducing depression symptoms. For instance, a recent study found that patients with major depression receiving aerobic exercise training performed either at home or in a supervised group setting achieved reductions in depression comparable to standard antidepressant medication (sertraline) and greater reductions in depression compared to placebo controls [7]. Interestingly, a different study reported that individuals with major depressive disorder undergoing an aerobic exercise program were as likely to be in remission as those taking standard antidepressant medication (sertraline) or medication and exercise combined [49]. These results are further supported by a study showing that a 4-month aerobic exercise program was more successful in reducing depression symptoms than a placebo and a pharmacological treatment [50]. In line with these findings, a recent study demonstrated that an 8-month exercise program was successful in improving depression symptoms in 40–60 year-old depressed women, unlike a pharmacological treatment [51].

Properties of exercise stimulus

Methodological limitations in existing research preclude a clear identification of the optimum exercise properties for treating depression [22]. However, it is important to acknowledge that the majority of relevant published evidence suggests an inverted dose–response relationship between exercise frequency and depression symptoms. More specifically, a recent study examined the efficacy of low-frequency (one aerobic session/week) and high-frequency (3–5 aerobic exercise sessions/week) exercise interventions for 8 weeks showing that high-frequency exercise interventions are more efficacious in reducing depression symptoms [40]. These findings are supported by a Finnish study of 3,403 adults which demonstrated that exercise frequency is inversely associated with depression symptoms and overall well-being [52].

Based on evidence published to date, the duration of exercise intervention is not clearly related to outcome [22]. On the other hand, some—but not all [43]—evidence supports that more intense exercise regimes lead to larger improvements in mood [53–55], while aerobic + resistance training appears to generate stronger effects than aerobic + flexibility training [53]. These results mirror the finding that dynamic and anaerobic exercises have a more potent effect on β-endorphin than resistance and aerobic exercises [39]. Individualized and group-based interventions appear to be equally beneficial for treating depression [40]. Moreover, several sources of data—but not all [22, 40]—show that supervised physical activity programs may produce more potent effects on depression than non-supervised programs [7, 56, 57]. These findings may be explained by the fact that depressed patients in unsupervised programs fail to sustain a high-enough interest in order to complete the prescribed intervention, as shown in a previous study [58].

Exercise and physical activity for treating depression in diseased individuals

Two previous studies examining the efficacy of exercise interventions as a treatment for depression in sedentary individuals with hypertension reported significant

reduction of depression symptoms [57, 59]. Previous work in cardiovascular disease patients has shown that adding high-intensity resistance training to an outpatient cardiac rehabilitation aerobic exercise program is more efficacious in improving mood and depression levels compared to adding flexibility training [53]. Moreover, aerobic exercise appears to be beneficial in improving depression symptoms and quality of life in patients recovering from a heart attack [60]. Therefore, there is some support to the notion that the beneficial effects of exercise and physical activity on anxiety and depression can reduce the risk for death from cardiovascular illnesses, obesity and osteoporosis in cardiovascular disease patients [61]. However, given that classic depression treatments (i.e., not based on exercise/physical activity) do not reduce the associated morbidity/mortality in cardiac patients [62, 63], the beneficial effects of exercise and physical activity on cardiovascular morbidity/mortality may be independent of their effects on depression.

Discussion

Based on the presented evidence, it becomes clear that exercise and physical activity have beneficial effects on depression symptoms that are comparable to those of antidepressant treatments. Research thus far is showing that exercise and physical activity can be used as therapeutic means for acute and chronic depression in the general population as well as in hypertensive and cardiovascular disease patients. In this light, the presented evidence supports that an exercise science specialist may need to complement the primary care physicians and mental health specialists in order to successfully tackle depression symptoms and episodes.

Notwithstanding the attention on the effects of exercise and physical activity on depression and the excitement for the new discoveries in this area, our knowledge on the biophysical mechanisms (e.g., β-endorphins) involved in the exercise-induced decrease of depression symptoms is incomplete. Moreover, methodological limitations in existing research preclude a clear identification of the optimum exercise properties for treating depression, while the risks and cost effectiveness associated with relevant interventions remain unknown. These topics should be addressed by future research in order to improve and/or standardize the exercise prescription for individuals with depression symptoms.

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