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EXERCISE FOR THE TREATMENT OF DEPRESSION AND ANXIETY

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ABSTRACT

Depression and anxiety are the most common psychiatric conditions seen in the general medical setting, affecting millions of individuals in the United States. The treatments for depression and anxiety are multiple and have varying degrees of effectiveness. Physical activity has been shown to be associated with decreased symptoms of depression and anxiety. Physical activity has been consistently shown to be associated with improved physical health, life satisfaction, cognitive functioning, and psychological well-being. Conversely, physical inactivity appears to be associated with the development of psychological disorders. Specific studies support the use of exercise as a treatment for depression. Exercise compares favorably to antidepressant medications as a first-line treatment for mild to moderate depression and has also been shown to improve depressive symptoms when used as an adjunct to medications. While not as extensively studied, exercise has been shown to be an effective and cost-efficient treatment alternative for a variety of anxiety disorders. While effective, exercise has not been shown to reduce anxiety to the level achieved by psychopharmaceuticals.

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Depression and anxiety are the most common psychiatric conditions seen in the general medical setting [1-5]. More than 340 million people worldwide are affected by depression [6]. Approximately 16% of the U.S. population will meet criteria for major depression in their lifetime, with women being 1.7 times more likely than men to develop the disorder [7]. Depression is the leading cause of disability worldwide and is predicted to be the second largest contributor to the global burden of disease by the year 2020 [8]. More than 30 million Americans have a lifetime history of anxiety, and anxiety disorders cost an estimated $42 billion per year in the United States [9, 10]. The most common types of anxiety disorders are generalized anxiety disorder, panic disorder, social anxiety disorder, and posttraumatic stress disorder [11-15].

The treatments for depression and anxiety are multiple and have varying degrees of effectiveness. Although options for pharmacologic treatment have expanded significantly in the past 20 years, between one- and two-thirds of patients will not respond to the first antidepressant prescribed, and 15 to 33% will not respond to multiple interventions [16-18]. Additionally, anxiolytic and antidepressant medications are expensive and associated with a number of serious and quality of life altering side effects.

Physical activity and exercise have been recommended for the prevention and treatment of numerous diseases and medical conditions (see Table 1). Most notably, habitual physical activity prevents the development of coronary artery disease and reduces symptoms in patients with established cardiovascular disease [19]. Evidence also supports the role of exercise in reducing the risk of other chronic diseases such as type 2 diabetes mellitus, osteoporosis, obesity, and cancer of the breast and colon. In addition, exercise and physical activity have been recommended for the treatment of depression and anxiety.

EXERCISE/PHYSICAL ACTIVITY AND BEHAVIORAL HEALTH

Studies have consistently noted that physical activity is associated with improved physical health, life satisfaction, cognitive functioning, and psychological well-being.

Table 1. Definition of Physical Activity and Exercise

Physical Activity	Bodily movement produced by skeletal muscles that results in energy expenditure beyond resting level.
Exercise	Subset of physical activity that is planned, structured, repetitive, and purposeful.

Early large population studies examined the relationship between exercise behavior and mental health [20, 21]. The relation between self-reported physical activity and depressive symptom was analyzed for 1,900 healthy subjects aged 25–77 years in the Epidemiologic Follow-up Study (1982–1984) to the first National Health and Nutrition Examination Survey (NHANES I) and found that physical inactivity may be a risk factor for depressive symptoms [20]. Weyer [21] found the odds ratio for depression to be significantly higher (OR 3.15) for the physically inactive compared to regular exercisers in a sample of 1,536 individual 15 years of age and older.

Subsequently, physical activity has been shown to be associated with decreased symptoms of depression and anxiety in numerous studies [22-25]. For example, in a nationally representative sample of adults ages 15–54 in the United States (n = 8,098), regular physical activity was associated with a significantly decreased prevalence of current major depression and anxiety disorders [26]. Physical activity was not found to be significantly associated with other affective, substance use, or psychotic disorders. In a study of 19,288 individuals, De Moor [27] found that regular exercise was associated with lower levels of depression, anxiety, and neuroticism.

Habitual exercise correlates to a heightened level of mental health and well-being and reduced feelings of anxiety regardless of the gender of the individual. In a group of men (n = 5,451) and women (n = 1,277), relative increases in maximal cardiorespiratory fitness and habitual physical activity are associated with lower depressive symptoms and greater emotional well-being [28]. Ohta [29] noted that 30 minutes or more of walking or cycling while commuting to work may be associated with an increased perception of mental health in men. In a study of 22,073 female college students ages 18-24, Adams [30] found that women who perceived their overall health as good, very good, or excellent were, respectively, 1.22, 1.78, and 2.61 times more likely to participate in regular cardiovascular exercise. Additionally, those who fit the same perception of health were 1.18, 1.57, and 2.03 times more likely to participate in strength training.

In contrast to gender, the age of the individual may affect the relationship between physical activity and mental health. Exercise has a very small but statistically insignificant effect on reducing anxiety in adolescents [31, 32]. In contrast, Fox [33] found that a population of European adults over the age of 70 had perceived levels of health and quality of life that were positively correlated to higher levels of physical activity.

While regular physical activity appears to be related to mental well-being, physical inactivity appears to be associated with the development of psychological disorders. Some cross-sectional and prospective-longitudinal clinical and epidemiological studies have shown a direct relationship between physical inactivity and symptoms of depression and anxiety [34].

POSSIBLE NEUROPHYSIOLOGIC MECHANISM

Physical activity and exercise have been shown to induce widespread neurobiological adaptations. Imaging studies have demonstrated structural changes associated with early onset depression in the hippocampus, amygdala, striatum, and frontal cortex; areas that are all extensively interconnected [35]. Most consistently associated with depression are the findings of volume loss in the hippocampal formation [36-38]. Increased levels of hippocampal brain-derived neurotrophic factor (BDNF) levels are associated with decreased anxiety [35].

As noted above, imaging studies have shown that depressed patients have decreased hippocampal volume [36]. Brain neurogenesis is increased by antidepressant medications [39]. Ernst and colleagues [40] hypothesize that exercise similarly decreases depressive symptoms by increasing brain neurogenesis. They outline four possible molecular mechanisms for this increased neurogenesis, all of which both promote hippocampal neurogenesis and increase with exercise: B-endorphins, vascular endothelial growth factor, brain-derived neurotrophic factor, and serotonin.

Other possible mechanisms for exercise's ability to improve mood include the association with exercise and increased levels of endocannabinoids, which are associated with analgesia, anxiolysis, and a sense of well-being [41]. Changes in the hypothalamopituitary adrenal axis, including increased adrenocorticotropic hormone (ACTH) and decreased cortisol production, are associated with exercise and thought to be part of the mechanism of its positive effects on mood [42]. Finally, exercise improves self-concept in depressed patients, possibly leading to decreased depressive symptoms [43].

TREATMENT OF DEPRESSION WITH EXERCISE AND PHYSICAL ACTIVITY

While studies support the use of exercise as a treatment for depression, exercise is rarely prescribed as a treatment for this common problem. In their depression treatment guidelines, the American Psychiatric Association (APA) states that exercise may be of value but does not consider it as a first line treatment [18]. The National Guideline Clearinghouse states in a consensus-based recommendation that exercise is recommended as an adjunctive treatment to antidepressants or psychotherapy [44].

Multiple studies exist that suggest that exercise is an effective treatment for depression. A Cochrane meta-analysis of 25 randomized controlled trials comparing exercise and placebo or a control intervention found that the exercise groups had a significant improvement in depressive symptoms when compared to the placebo or control group [45]. Only three trials with sufficient allocation concealment, intention to treat analysis, and blinded outcome assessment were found (see Table 2). When these three trials were analyzed together, the effect size was not significant.

Table 2. Exercise in the Treatment of Depression

Study	Participants/intervention	Primary outcome	Results
Mather, 2002 [25]	Adults (n = 86) diagnosed with depression randomized to exercise group (predominately weight-bearing exercise lasting 45 minutes, twice weekly for 10 weeks) or control group (health education).	Proportion of participants achieving a "response," defined as a ≥ 30% reduction in Hamilton Rating Scale for Depression (HRSD).	At 10 weeks a significantly higher proportion of the exercise group (55% v. 33%) experienced a greater than 30% decline in depression according to HRSD.
Dunn, 2005 [46]	Adults (n = 80) diagnosed with mild to moderate MDD randomized to one of four aerobic exercise (treadmill or stationary bicycle) treatment groups that varied total energy expenditure (7.0 kcal/kg/week— lower dose or 17.5 kcal/kg/week— higher dose) and frequency (3 days/ week or 5 days/week) or to exercise placebo control (3 days/week flexibility exercise).	Change in the HRSD score from baseline.	The main effect of energy expenditure in reducing HRSD scores at 12 weeks was significant. Adjusted mean HRSD scores at 12 weeks were reduced 47% from baseline for higher dose of exercise, compared with 30% for the lower dose and 29% for control. There was no main effect of exercise frequency at 12 weeks.
Blumenthal, 2007 [47]	Adults (n = 202) diagnosed with MDD were randomized to one of four conditions: supervised exercise (treadmill) in a group setting; home-based exercise; antidepressant medication (sertraline, 50-200 mg daily); or placebo pill.	Percentage of patients achieving remission as defined as no longer meeting the criteria for MDD and a HRSD score of < 8.	After 4 months of treatment, 41% of the participants achieved remission. Patients receiving active treatments tended to have higher remission rates than the placebo controls; supervised exercise = 45%; home-based exercise = 40%; medication = 47%; placebo = 31% (p = .057). All treatment groups had lower HRSD scores after treatment; scores for the active treatment groups were not significantly different from the placebo group (p = .23).

Exercise compares favorably to antidepressant medications as a first-line treatment for mild to moderate depression. Blumenthal [48] conducted a randomized controlled trial in which they assigned 156 adults over age 50 to either aerobic exercise, sertraline, or both. After 4 months, all three groups had a statistically significant improvement in their depressive symptoms with no statistically significant difference between the groups. The medication group did have a faster response to treatment in the first 4 weeks. In a more recent study, Blumenthal [47] found significantly improved symptoms with remission rates of 45% in a supervised exercise group, 40% in a home-based exercise group, 47% in a medication group, and 31% in a placebo group. The differences between the intervention and placebo groups were not statistically different.

Exercise has also been shown to improve depressive symptoms when used as an adjunct to medications. Exercise significantly improved symptoms when added to an antidepressant in a group of older patients with depression that had not responded to 6 weeks of antidepressant medication alone [46]. Unlike its benefit as an adjunct to antidepressive medications, exercise in addition to cognitive therapy was found to be no better than either alone [49].

A dose-response effect with exercise in the treatment for depression has been noted. In one study, high intensity weight training was more effective than low intensity weight training in treating depression [50]. Low intensity weight training and general practitioner care were found to have nearly the same improvement in depression that is consistent with the widely accepted number of the 30% placebo effect in depression treatment. With aerobic exercise, intensity equaling the energy expenditure in public health recommendations was more effective than a program of guided movements of low intensity that had a reduction in depressive symptoms equal to the placebo group [51].

While more research is needed on the type of exercise needed for depression treatment, available research indicates that the type of exercise is not as important as having the physical activity reach a sufficient intensity. For example, both running and weight lifting were found to significantly decrease depressive symptoms with no significant difference found between these two forms of physical activity and the decrease in symptoms [52].

TREATMENT OF ANXIETY WITH EXERCISE AND PHYSICAL ACTIVITY

Compared to the wide range of research on the positive effects of exercise on depression, anxiety disorders have been less frequently studied [33]. In general, aerobic exercise has been shown to be an effective and cost-efficient treatment alternative for a variety of anxiety disorders [53]. Several studies have indicated that aerobic exercise may be as effective in reducing generalized anxiety as cognitive behavioral therapy [54].

In treating anxiety, exercise has been shown to alleviate anxious feelings. Exercising at 70%–90% of maximum heart rate for 20 minutes three times a week has been shown to significantly reduce anxiety sensitivity [55]. Self-reported fears of anxiety sensations, fears of respiratory and cardiovascular symptoms, publicly observable anxiety symptoms, and cognitive dyscontrol decrease following a prescribed exercise program [56]. In a study by Cox and colleagues [57], the most substantial decrease in state anxiety occurred 90 minutes following 20 minutes of aerobic exercise at 80% of maximal oxygen uptake.

While useful in treatment, exercise has not been shown to reduce anxiety to the level achieved by psychopharmaceuticals. In a study of patients suffering from moderate to severe panic disorder, both a 10-week protocol of regular aerobic exercise and clomipramine were associated with significant improvement of symptoms compared to placebo [58]. In comparison with exercise, clomipramine improved anxiety symptoms more effectively and significantly earlier.

In general, exercise does appear to be effective in reducing symptoms associated with anxiety (see Table 3). Furthermore, symptoms improve following both an acute episode of physical activity as well as following a program of routine exercise.

RISKS OF PHYSICAL ACTIVITY AND EXERCISE

While the Center for Disease Control and Prevention and the American College of Sports Medicine recommend that individuals should engage in 30 minutes or more of moderate-intensity physical activity on most (preferably) all days of the week [59], physical activity and exercise have risks that need to be considered. The most common risk of physical activity in adults is musculoskeletal injury [60, 61]. The risk of injury increases with obesity, volume of exercise, and participation in vigorous exercise such as competitive sports [18]. Furthermore, vigorous physical activity acutely increases the risk of sudden cardiac death and myocardial infarction among individuals with both diagnosed and occult heart disease.

CONCLUSION

Depression and anxiety disorders are some of the most prevalent neurological disorders in the United States, with as many as 18% of adults demonstrating symptoms. Exercise has been shown to reduce symptoms associated with these disorders and has the potential to lessen the dependability on psychopharmacology.

Physicians should recommend that adults participate in at least 30 minutes of accumulated moderate-intensity physical activity (for example, walking fast) on most days of the week. As noted by Meriwether and colleagues [62], the key principles for physical activity are as follows:

Table 3. Exercise in the Treatment of Anxiety

Study	Participants/intervention	Primary outcome	Results
Brooks et al., 1998 [58]	Patients (n = 46) with moderate to severe panic disorder with or without agoraphobia (DSM-III-R criteria) were randomly assigned to a 10-week treatment protocol of regular aerobic exercise (running), clomipramine (112.5 mg/day), or placebo pills.	Change in scores for following scales from baseline: Hamilton Anxiety Rating Scale, observer-rated and patient-rated versions of the Panic and Agoraphobia Scale, observer and patient versions of the Clinical Global Impression, and the Fear Questionnaire.	Both exercise and clomipramine led to a significant decrease in symptoms according to all main efficacy measures (analysis of variance, last-observation-carried-forward method and completer analysis). A direct comparison of exercise and clomipramine revealed that the drug treatment improved anxiety symptoms significantly earlier and more effectively. Depressive symptoms were also significantly improved by exercise and clomipramine treatment.
McEntee & Haglin, 1999 [54]	Participants (n = 70) were divided into four groups: cognitive group therapy, aerobic exercise, both treatments, or control.	Change in State-Trait Anxiety Inventory	All interventions were equally effective in reducing anxiety as compared to no intervention. The combination of cognitive group therapy and exercise was not significantly more effective than either cognitive group therapy or aerobic exercise alone.

Cox et al., 2004 [57]	Participants (n = 24) completed a non-exercise control condition as well as one exercise bout at 60% and 80% maximal oxygen uptake.	Change in Spielberger State Anxiety Inventory.	All three exercise conditions (including control) showed a decline in state anxiety across time.
Smits et al., 2008 [55]	Participants (n = 60) with elevated levels of anxiety sensitivity were randomized to a 2-week exercise intervention, a 2-week exercise plus cognitive restructuring intervention, or a waitlist control condition.	Change in the fear of anxiety-related sensations (anxiety sensitivity).	Both exercise conditions led to clinically significant changes in anxiety sensitivity that were superior to the waitlist condition. Adding a cognitive component did not facilitate the effects of the exercise intervention.
Broman-Fulks & Storey, 2008 [56]	Participants (n = 24) with high anxiety sensitivity scores (Anxiety Sensitivity Index-Revised scores > 28) were randomly assigned to complete either six 20-minute sessions of aerobic exercise or a no-exercise control condition.	Change in Anxiety Sensitivity Index-Revised.	Individuals assigned to the aerobic exercise condition reported significantly less anxiety sensitivity subsequent to exercise, whereas anxiety sensitivity scores among non-exercisers did not significantly change.

1. the more activity the better;
2. accumulated time is more important than intensity;
3. activity can be accumulated in 10-minute increments; and
4. lifestyle activities (e.g., substituting walking or biking for short car rides, using a push rather than a riding lawn mower) are more likely to be sustained than structured activities such as exercising at a gym.

Using the five As (Assess, Advise, Agree, Assist, Arrange) model has often been recommended as a tool to assist physicians in providing a patient-specific exercise recommendation.

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