Exercise is Medicine

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Exercise, Depression, and the Brain

Exercise is now understood to dramatically effect mood and produce positive clinical changes in depression. Research over the last ten years in both humans and animal models has shown the antidepressive mechanism of exercise. Exercise can affect key brain neurotransmitters as well as prolong the life of neurons through stimulation of neurotrophic factors. These mechanisms, as well as the growing body of research showing that movement is a reliable antidepressant, provide insight into combating the leading cause of morbidity in the Western world.

Exercise's Impact on the Brain

Studies using animals have shown that exercise can activate key neurotransmitters involved in mood.[1] Both serotonin (5-HT) and norepinephrine (NE) are monoamines used in antidepressant medications. Serotonin reuptake inhibitor drugs (SSRI), such as Prozac, are often the first medications prescribed by doctors treating depression. When these therapies do not provide adequate response, combination medications are used. Serotonin norepinephrine reuptake inhibitor (SNRI) medications, such as Effexor, modulate both serotonin and norepinephrine. While SSRI and SNRI medications can provide much-needed relief to some patients, clinical trials have shown that 40% to 50% of depressed patients are unresponsive to first-time treatment.[17] In addition, there are sometimes unwanted side effects from these medications. Exercise is able to address depression by altering these same neurotransmitters more quickly and without side effects.[1,4,13]

Chronic exposure to wheel-running in rat models raises serotonin levels in several key areas of the brain (hippocampus, amygdala, and locus coeruleus).[3] In addition, the impact of exercise on serotonin levels occurs quickly and can be shown in cerebrospinal fluid as well.[4,8] The same is true for norepinephrine. It is also increased by chronic aerobic exercise, although the effects are more delayed.[7] Both norepinephrine and serotonin are important brain-signaling molecules for depression. They have both been shown to not only enhance mood, but also increase neuronal health by extending nerve survival rates, improve "synaptic plasticity," and stimulate neural repair.[4–6] However, exercise acts even more globally on neurotransmission. In addition to its action on serotonin and norepinephrine, movement also enhances GABA, acetylcholine, and dopamine neurotransmission.[2,9] The global impact of this enhanced neurotransmission is the key to the antidepressant effect of exercise.

The neurotrophic hypothesis of depression is quickly gaining widespread support. Research has shown that decreased neurogenesis increases the risk of depression.[10] It is also now hypothesized that antidepressants work via global neurological mechanisms that go beyond neurotransmitter action.[14] This has lead to the recognition that BDNF (brain-derived neurotrophic factor) may be the key player in depression and a common mechanism of action between exercise and antidepressant medication. BDNF is a member of a family of compounds called neurotrophins, which are secreted proteins that signal neurons to grow, evolve, and survive. In animal models, BDNF increases neurogenesis and protects existing neurons from damage. Exercise has been shown to stimulate BDNF, and this effect is mediated through the enhanced neurotransmission induced by movement.[2,9–11,14] Norepinephrine seems to be the most important BDNF modulator shared by exercise and some antidepressants.[4] However, exercise has more "holistic" action on the brain, modulating not only serotonin and norepinephrine, but also GABA, dopamine, and acetylcholine. This may explain the quicker treatment response and lack of side effects with exercise as compared with pharmaceutical intervention.[2,9,11]

Exercise and Depression Studies

A 2006 meta-analysis published in the journal *Psychology of Sport and Exercise* analyzed the results of over 150 studies and 3000 participants.[12] This study showed that low-intensity aerobic exercise of only 30 minutes' duration had statistically significant and clinically meaningful results for depression. The most important

aspect of the study was to clear up the confusion that had remained in the literature as to whether exercise created improved mood, or that improved mood simply was correlated with increased exercise. In this review of the literature, exercise was shown to have a druglike impact on mood for up to 30 minutes after an acute exercise bout.

Several studies demonstrate that exercise works for both prevention and treatment of depression.[13–15] A 2001 study in the *British Journal of Sports Medicine* showed that individuals with major depression who started a walking program for 30 minutes daily had statistically significant improvements in mood in just over 10 days.[13] Even subjects who were previously unresponsive to pharmaceutical intervention showed improvement from walking.

In 2000 researchers compared exercise directly against pharmaceutical intervention. This study looked at 156 adult subjects with major depression over a 12-month period. Subjects were randomized to drug therapy (SSRI Zoloft), exercise and drug therapy, and exercise alone. The exercise intervention had subjects doing moderate-intensity activity on a treadmill three times per week. The exercise only group had better results for treatment effect, remission, and relapse than the Zoloft group or the Zoloft and exercise group.[16]

Final Thoughts and Prescription

From the research, it is clear that exercise can provide a global tonic to brain neurotransmission. This effect directly affects mood and acts as an antidepressant, but also has more global brain impact through the induction neurotrophic factors which enhance brain neurotransmission further, as well as prolong the life and improve the function of individual neurons. Given its quick response rate against even severe depression as well as its lack of side effects and holistic action on other organ systems, exercise prescription should be regarded as a primary intervention for depression.

The research on exercise and depression has centered almost exclusively on aerobic exercise. The most robust response comes from low- to moderate-intensity aerobic exercise. The key in most exercise studies focuses on consistency. To deal with constraints of time and aversion to exertion, a 30-minute walking program on all or most days of the week would likely provide the most clinical benefit and fewest obstacles. Japanese research has shown a benefit of walking in the outdoors in a "nature setting" over urban or gym environments.[18]

Notes

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