Impact of Aerobic Exercise on Depression

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Disclosures

• The Speakers have no Financial or Industry Disclosures
• No off-label medication use is discussed
Background

• Overview of Major Depressive Episodes
• Treatment of Depression in Athletes
• Running/aerobic exercise as treatment for depression
Major Depressive Episodes

• MEDICAL CONDITION ASSOCIATED WITH CORONARY HEART DISEASE, HYPERTENSION AND DIABETES

• FOUND TO BE AN INDEPENDENT RISK FACTOR FOR DM2 AND HTN

• ASSOCIATED WITH LOW PHYSICAL ACTIVITY BUT MULTIPLE STUDIES FIND THE HAVING DEPRESSION ALONE INCREASES RISK FOR CAD AND METABOLIC PROBLEMS

• STRONG ASSOCIATION WITH COMPLETED SUICIDE
MDE-Key Clinical Features

*Prolonged Low Mood, Sadness and or Depressed Mood*-often lasting weeks or longer, expression of mood varies with culture and other demographics.

*Loss of the capacity to feel pleasure*-other people often notice this first-not smiling or laughing, lack of interest in work or hobbies

Associated with:

- change in appetite or unexplained weight loss or gain
- inattention
- disrupted sleep
- excessive guilt
- delusions
- hallucinations
- suicidal thoughts
Depression Screening

The **Patient Health Questionnaire-9 (PHQ9)** is validated for screening, aid in diagnosis and treatment response

A short version of the PHQ9 (the PHQ2) is 85% sensitive for major depression

- 0=none, 1=less than 1/2 the days, 2=half the days, 3 everyday or almost every day
- Little interest or pleasure in doing things the past 2 weeks: 0 1 2 3
- Feeling down depressed or hopeless the past 2 weeks: 0 1 2 3
Rates of Mood Disorders in Runners

- Lifetime rate of MDE for adults is 15-20% in general population
- Studies are limited in athletes but the rate of MDE is similar to general population with some difference in risk factors:
  - Overtraining, injury, aging and retirement from sport
  - Rates are very high in NFL (American Football) players
- ULTRA Study Data on Prevalence of Depression Anxiety and Drug Abuse
- Reported Medical Conditions:
  - Depression and bipolar disease: 11.8%
  - Anxiety 7.8%
  - Alcohol and drug abuse 3.4%
- There is an overlap of Overtraining Syndrome and Major Depression
Treating Depression in Athletes

- There are a small number of studies looking at the impact of treating athletes with antidepressants on performance.
- SSRI’s (Lexapro Prozac), SNRI’s (Effexor) and Bupropion (Welbutrin) do not have significant effect on performance. Combining antidepressants with exercise may have an synergistic effect on reducing depression severity.
- WADA has investigated Bupropion as a possible PED but multiple studies have a small n and mixed results.
- Tricyclic Antidepressants (Amitriptyline, Nortriptyline) have significant cardiac side effects and anticholinergic activity that can have a negative impact on training and athletes treated with these medications should be closely monitored by experienced healthcare professionals.
Aerobic Exercise as Treatment for Depression
Evidence/Research

• Clinical Trials
• Comparison to other treatments
• Basic science/physiologic mechanisms
Clinical Studies

• Moderate aerobic exercise for at 30-40 minutes a day, 4 days a week for 2-3 months has significant effect in reducing the symptoms of depression.


  • B Stubbs, D Vancampfort, Challenges Establishing the Efficacy of Exercise as an Antidepressant Treatment: A Systematic Review and Meta-Analysis of Control Group Responses in Exercise Randomised Controlled Trials. Sports Med Springer International Publishing Switzerland 2015
Clinical Evidence

• Over 32 Clinical Trials and several open trials examining effect of exercise on depression
• Overall there is a moderate positive effect on MDE
• 2 RCT trials found no difference in remission rates compared to medications in moderate depression
• Larger impact on elderly
• Reduces the symptoms of depression in patients with co-morbid CAD
Meta-Analysis

- Data from 25 RCT
- Found larger effect than previous studies and Cochrane reviews
- Pooled data found difference in intensity and structure
- Moderate to Intense Aerobic Exercise had largest affect on reducing depression
- Supervised exercise interventions were more effective
- Indicates previous studies may have underestimated the efficacy of aerobic exercise in treatment of Major Depressive Episodios
How does exercise cause and antidepressant effect?
Adiponectin

Adiponectin, is secreted by peripheral mature adipocytes during physical exercise—the hormone stimulates hippocampal neurogenesis and is found reduce depression in animal models

Schematic diagram illustrating the potential mechanism mediating the anti-depressive action of physical exercise.

As shown in this cartoon, physical exercise initially raises circulating adiponectin levels. The low-molecular-weight (LMW) form of adiponectin passes through the blood-brain barrier, and accumulates in the hippocampus to activate adiponectin receptor (ADNR) 1 expressed by neural progenitor cells. Following the relay of adapter protein containing PH domain, PTB domain and leucine zipper motif 1 (APPL1), the phosphorylated AMP-activated protein kinase (p-AMPK) is increased, subsequently initiating the downstream proneurogenic cascade that enhances hippocampal cell proliferation without affecting neuronal differentiation. The enlarged population of adult-born neurons changes the activity of neural circuits and enables the antidepressant effects elicited by physical exercise. Brain-derived neurotrophic factor (BDNF) and insulin-like growth factor (IGF-1) do not seem to directly crosstalk with this adiponectin-stimulated proneurogenic pathway.
5-HT2C Receptors in the Basolateral Amygdala and Dorsal Striatum

• Activation of these serotonin receptors found to have an antidepressant and anxiety reducing activity in animal models
• Exercise found to both increase up regulation of 5HT$_{2c}$ in the Amygdala and Dorsal Striatum
• Exercise also increased sensitivity of those receptors
Hypocretin/Orein Suppression

Antidepressant effects of exercise are produced via suppression of hypocretin/orexin and melanin-concentrating hormone in the basolateral amygdala. T.-K. Kim et al. / Neurobiology of Disease 79 (2015) 59-69

• In mice model of depression, mice with vigorous exercise had significantly shorter duration of illness
• Immunohistochemistry found significant suppression of hypocretin/Orein and MCH
Brain Derived Neurotrophic Factor

• Aerobic Exercise found in several well designed studies to increase both serum and CSF BDNF
• No association with increased heart disease with the elevated BDNF
• One RTC found in depressed patients randomized to structured exercise and usual care had both increased BDNF over control and improved Depressive symptoms
Integrating Exercise Into Practice

• Motivating patients
• Creating an integrated training plan
• Risk assessment of patients
Motivation

- 12 studies met inclusion criteria with an n=6431
- Study questioned motivations and barriers to exercise in those with mental illness

**Motivations:**
- Fitness
- Weight loss
- Improve mood
- Reduce stress

**Barriers:**
- Lack of supervision during exercise
- Mood symptoms
Summary

• Depression is a serious medical condition that is often not recognized and treated
• There are evidence based and effective treatment options including pharmacologic and non-pharmacologic interventions
• Aerobic Exercise can be an effective treatment for Major Depressive Episodes if they are supervised and motivations and barriers to exercise are addressed
References


Antidepressant effects of exercise are produced via suppression of hypothalamus/orcin and melanin-concentrating hormone in the basolateral amygdala. Tae-Kyung Kim et al. Neurobiology of Disease 79 (2015) 59-69


Psychiatric medication preferences of sports psychiatrists. Claudia L. Reardon & Shane Creado. THE PHYSICIAN AND SPORTS MEDICINE, 2016. VOL. 44, NO. 4, 397-402
QUESTIONS