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Take Control of Your Health

Study: Exercise Should Be First Treatment for Depression

Analysis by Dr. Joseph Mercola ✔ Fact Checked | March 16, 2023

STORY AT-A-GLANCE

- An overview of 97 systematic reviews and meta-analyses found exercise is 1.5 times more effective for mental health than top medications or counseling, and benefits were seen in 12 weeks
- The authors of the umbrella review call on mental health professionals and doctors to start prescribing exercise as a first line of treatment
- Another systematic review, which analyzed the association between physical activity and the risk of depression, found there's a dose-dependent response. Compared to those who did not exercise, people who got half the recommended volume of physical activity lowered their risk for depression by 18%. Those who got the recommended amount lowered their risk by 25%
- Most health authorities recommend getting 150 to 300 minutes of moderate intensity activity or 75 to 150 minutes of vigorous intensity exercise each week
- Previous research has also found that people who met or exceeded the weekly exercise recommendation lowered their risk of death. Men can lower their risk of cardiovascular disease death by as much as 34% and their all-cause mortality by up to 36%; women can lower their CVD death risk by as much as 44% and their all-cause mortality by as much as 55%

I've been a long-term advocate for exercise as a primary treatment option for depression, and now, an overview of systematic reviews[1,2,3] shows just how well-reasoned this advice has been.

Exercise Is 1.5x More Effective Than Best Antidepressants

In all, 97 systematic reviews with meta-analyses of controlled trials assessing the effects of exercise on adult depression, anxiety and psychological distress were included (amounting to a total of 1,039 trials involving 128,119 participants).

Populations included healthy adults, people with mental health disorders and people with chronic diseases. It's the most comprehensive review of research to date, and clearly demonstrates that exercise can rapidly alleviate mild to moderate symptoms of depression, anxiety and other forms of psychological distress. As reported by the University of South Australia, which performed the umbrella review:[4]

> *"University of South Australia researchers are calling for exercise to be a mainstay approach for managing depression as a new study shows that physical activity is 1.5 times more effective than counselling or the leading medications …*
>
> *[The study] shows that physical activity is extremely beneficial for improving symptoms of depression, anxiety, and distress. Specifically, the review showed that exercise interventions that were 12 weeks or shorter were the most effective at reducing mental health symptoms, highlighting the speed at which physical activity can make a change.*
>
> *The largest benefits were seen among people with depression, pregnant and postpartum women, healthy individuals, and people diagnosed with HIV or kidney disease … Lead UniSA researcher, Dr Ben Singh, says physical activity must be prioritized to better manage the growing cases of mental health conditions.*
>
> *'Physical activity is known to help improve mental health. Yet despite the evidence, it has not been widely adopted as a first-choice treatment. Our review shows that physical activity interventions can significantly reduce symptoms of depression and anxiety in all clinical populations, with some groups showing even greater signs of improvement.*

Higher intensity exercise had greater improvements for depression and anxiety, while longer durations had smaller effects when compared to short and mid-duration bursts.

We also found that all types of physical activity and exercise were beneficial, including aerobic exercise such as walking, resistance training, Pilates, and yoga. Importantly, the research shows that it doesn't take much for exercise to make a positive change to your mental health.'"

Dose-Response Association Between Exercise and Depression

Another systematic review,[5] published in April 2022, which analyzed the association between physical activity and the risk of depression, found there's a dose-dependent response. This review included studies from around the world published up until December 2020. In all, 15 studies were included, with a total of 191,130 participants.

> **“Compared to those who did not exercise, people who got half the recommended volume of physical activity lowered their risk for depression by 18%. Those who got the recommended amount lowered their risk by 25%.”**

All studies included assessed the effects of at least three different exposure levels and had a follow-up of at least three years. Compared to those who did not exercise, people who got half the recommended volume of physical activity lowered their risk for depression by 18%. Those who got the recommended amount lowered their risk by 25%.

> **“... if less active adults had achieved the current physical activity recommendations, 11.5% of**

> **depression cases could have been prevented. ~ JAMA Psychiatry”**

The World Health Organization recommends getting 150 to 300 minutes of moderate intensity activity or 75 to 150 minutes of vigorous intensity exercise each week, and that is the exercise volume they're referring to. According to the authors:

> *"… if less active adults had achieved the current physical activity recommendations, 11.5% of depression cases could have been prevented … Health practitioners should therefore encourage any increase in physical activity to improve mental health."*

The Science Behind Exercise's Mood-Lifting Effects

In this short video, Rhonda Patrick, Ph.D., a biomedical scientist and researcher formerly with the Salk Institute for Biological Sciences in La Jolla, California, discusses the science behind the **mood-lifting effects of exercise**.

One of the ways exercise promotes mental health is by normalizing insulin resistance. Mechanistic studies, several of which are highlighted in Patrick's video, have also linked the antidepressant effects of exercise to molecular mechanisms involving:

- Kynurenine, a neurotoxic stress chemical produced from the amino acid tryptophan — As explained by Patrick, tryptophan is an essential amino acid required for the synthesis of serotonin, melatonin, vitamin B3 and kynurenine. While kynurenine is associated with stress and depression at higher levels, higher levels of serotonin are associated with improved mood.

  To a degree, exercise will allow you to control what the tryptophan will be synthesized into. By allowing for more tryptophan to be transported into your brain, exercise raises your serotonin and inhibits conversion into kynurenine, thereby boosting mood and preventing depression.

Animal research[6] has also shown that well-trained muscles have higher levels of an enzyme that helps metabolize kynurenine, thereby ridding the body of it.

- Myokines — Myokines are cytokines produced by your muscles, and while cytokines are typically inflammatory, myokines are anti-inflammatory. They also increase your insulin sensitivity by improving glucose utilization inside your muscles and, acting as chemical messengers, they help inhibit the release of inflammatory cytokines produced by body fat.
- Brain-derived neurotrophic factor (BDNF), a growth factor that regulates neuroplasticity and new growth of neurons.
- The endocannabinoid system — While runner's high is typically attributed to the release of endorphins, running also dramatically increases anandamide, an endogenous cannabinoid, in your body, which influences your opioid and endorphin receptors.

  The higher your anandamide level, the better you feel. Research[7] shows people engaging in moderate intensity running or cycling increase their anandamide levels, and that the greatest increase occurs when you're exercising at 70% to 80% of your maximum heart rate.
- Beta endorphin, an endogenous opioid neuropeptide and peptide hormone.

Exercise and Longevity

Exercise also has a significant impact on longevity. Several studies have confirmed that people who get at least 150 minutes — 2.5 hours — of exercise live significantly longer than those who don't exercise.

For example, one 2014 study[8] found men who met or exceeded the recommendation of at least 150 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity lowered their risk of cardiovascular disease (CVD) death by as much as 34% and

their all-cause mortality by as much as 36%. Women who met the guidelines lowered their CVD death risk by up to 44% and all-cause mortality by as much as 55%.

Interestingly, when it comes to the question of which intensity is most beneficial, this study found the answer must take your gender into account. As reported by the authors:

> *"When comparing different combinations of moderate- and vigorous-intensity activity and all-cause mortality rates, we observed sex-related differences.*
>
> *Holding constant the volume of moderate- to vigorous-intensity physical activity, men experienced a modest additional benefit when expending a greater proportion of moderate- to vigorous-intensity physical activity in vigorous-intensity activities, but women did not."*

Do Weekend Warriors Get the Same Benefits?

Oftentimes, people complain they can't carve out 30 minutes a day to exercise. Some try to make up for it by exercising for longer periods on the weekend. But does this still provide the same benefits? According to a 2022 study[9] of 350,978 individuals, the answer is yes.

There was no significant difference in mortality between those who squeezed in their exercise on the weekends and those who stayed active on a more daily basis. Both had lower all-cause mortality and cause-specific mortality rates.

Exercise Sustains Health in Myriad Ways

Since exercise extends your life span, it makes sense that it helps sustain health and reduces diseases that lead to premature death. A paper[10] published in the Journal of Sport and Health Science in January 2023 reviews the many ways in which exercise accomplishes this.

As noted in this paper, "The health benefits of exercise lies in the remarkable integrative adaptation of multiple tissues and organs," and "Regular exercise is considered a non-pharmacological polypill for patients with certain comorbidities." Importantly, it also helps protect your health when you're under stress.

The authors review how moderate-intensity exercise affects the major hallmarks of health, including the following. For more information about each one, please see the original paper:

Barrier integrity (mitochondria, plasma membranes, nuclear envelope, blood-brain-barrier, gut, intestinal, skin and respiratory tract)	Containment of local perturbations
Recycling and turnover	Integration of circuitries
Rhythmic oscillations	Homeostatic resilience
Hormetic regulation	Repair and regeneration

Best Exercise for Aging Bodies

Unfortunately, many people still equate "exercise" with aerobic-type exercise only (such as walking, jogging, swimming and biking, for example), forgetting about or ignoring the importance of strength training. Having muscle mass is incredibly important for optimal health, and only grows in importance as you age.

For an in-depth review of the benefits of maintaining strong muscles, see my January 2023 article "**How to Stay Fit for Life**," and my April 2022 **interview with Dr. Gabrielle Lyon**.

As explained in that interview, muscle mass is the key to longevity as it helps address such a wide range of health problems, from obesity and diabetes to heart disease and

Alzheimer's. In short, the greater your muscle mass, the higher your survivability against all diseases becomes.

One of the reasons for this is because you need protein reserves to survive serious disease, and most of your protein reserve is stored in muscle. If you have very little muscle, you're going to pass away prematurely because you have no amino acid reserves.

Your muscle also interfaces with your immune system, which is your first line of defense against most diseases, including cancer, and plays a major role in metabolism, circulation and cognition.

While you would ideally engage in all four types of exercise — endurance, strength, balance and flexibility[11] — if you're short on time, your best bet is to focus on strength training. In "**How to Stay Fit for Life**" I explain the unique benefits of blood flow restriction (BFR) training, which can be done using just your bodyweight or very light weights. This makes it ideal even for the elderly.

The BEST Strategy I Know of to Increase Muscle Size

There are loads of ways to increase your muscle mass but they mostly involve moving, pushing or pulling heavy weights or resistance bands. The problem with this strategy is that if you are not in good shape, and especially if you are elderly, there is a very high likelihood that you will get injured.

BFR or KAATSU is the answer to this problem. As the name implies, BFR involves modifying the arterial inflow and venous outflow while you're working the muscle by placing an inflatable band around the extremity. It is not like a tourniquet that stops all your blood flow, which is dangerous.

For clarity, KAATSU refers to the original method of BFR and uses a device that inflates your cuffs at specific intervals. The inflation and deflation that you get when using the KAATSU device not only makes it safer but also triggers physiological stimuli that are very difficult to reproduce without it.

Conventional resistance training typically uses resistance at 70% to 85% of your one-rep max, i.e., the maximum amount of weight you can lift only one time. Since this weight is relatively heavy and close to your limit, injuries are almost guaranteed.

BFR, on the other hand, is a low-intensity resistance training, using weights that are just 20% to 35% of your one-rep max. With weights this light, your risk of injury is largely eliminated. In many elderly and frail individuals, weights of just 1 or 2 pounds, or no weight other than your body, are all that is needed to achieve the benefits.

BFR's ability to achieve such remarkable physiological benefits is directly related to slowing venous blood flow from the muscle group being engaged and creating a relatively hypoxic environment or low oxygen pressures in the exercising muscle.

With very light exercise, and in about 15 to 20 minutes, you get an exhaustive workout that sends a signal to your brain that says, "Hey, I've done something really hard here — you better help me recover and adapt to it."

Your brain then sends out hormonal responses that cause your muscles and blood vessels to grow. Most would think that such light weights would be insufficient to provide any muscle strength improvements, but studies show a 36% to 40% increase in muscle strength after only 12 weeks,[12] depending on your load and health. For further details on how to do BFR and use the KAATSU system, see "**How to Stay Fit for Life**."

BFR Helps Improve Cognition — and Likely Depression As Well

To end where we began, on the issue of improving mental health with exercise, research favors BFR here as well, when compared to conventional strength training. As explained in a 2018 paper,[13] while resistance training has generally been shown to be less effective than aerobic exercises when it comes to improving cognitive performance on the behavioral and socioemotional level (e.g., decreased symptoms of depression and anxiety), BFR is different.

BFR, especially when you're using the KAATSU device, triggers a series of physiological responses that do not occur during conventional strength training, and several of these

have a direct impact on cognition. As explained by the authors:

> *"… systemic hypoxia leads to an oxygen deficit directly in the brain which is to a certain extent the decisive stimulus triggering positive neurophysiological adaptations …*
>
> *Based on the first hint that localized hypoxia is beneficial for cognition, we want to outline several reasons why localized hypoxia during a resistance training (e.g., trough BFR) might be a promising intervention strategy which is likely to increase the efficiency of resistance training regarding the enhancement of cognitive functions in the following:*
>
> *On the cellular and molecular level: Some investigations showed a significant higher release of hormones which is associated with positive neurophysiological adaptations, such as serum IGF-1, growth hormone (GH) and vascular endothelial growth factor (VEGF), in response to acute resistance activities with BFR when compared to resistance training without BFR.*
>
> *Regarding the IGF-1, also a long-term intervention (two weeks) of low-intensity BFR training which was provided twice a day led to a higher basal level of IGF-1 in comparison to the same resistance training without BFR … IGF-1 plays an important role in synaptic functioning and cognitive processes.*
>
> *Because of the link between a deficiency in serum GH level and a cognitive impairment, increases in GH are associated with benefits for cognitive performance … VEGF is involved in angiogenesis and it is speculated that a decrease in angiogenic factors (e.g., serum VEGF) might be associated with cognitive impairments …*
>
> *Furthermore, there is a robust body of evidence suggesting that the blood lactate concentrations are higher after an acute bout of resistance activities with BFR as compared to a resistance exercise without BFR. The levels of post-exercise blood lactate concentration are associated with acute improvements in cognitive functions such as short-term memory and executive functions.*

This phenomenon occurs because peripherally expressed lactate can cross the BBB by monocarboxylate transporters (MCTs) and will be utilized as fuel for cognitive processes due to oxygenation.

Moreover, lactate is associated with changes in peripheral brain-derived neutrophic factor (BDNF) … BDNF is a member of neurotrophins and contributes to neuroplasticity which, in turn, facilitates cognitive performance.

In addition, systemic hypoxia as well as local hypoxia increase the hypoxia-inducible factor 1α (HIF-1α) which is the master regulator for adaptions of oxygen homeostasis. An increase of HIF-1α in response to systemic and/or localized hypoxia (e.g., induced by BFR) might be meaningful for cognition or the integrity of the brain considering the following two aspects:

Firstly, the HIF-1α has a neuroprotective effect and secondly, this transcription factor triggers the increase of neurotrophic factors such as the VEGF and IGF-1. Therefore, the HIF-1α may be also a crucial factor for neurocognitive adaptations following a resistance training with BFR."

On the functional level, BFR has also been shown to increase cortical activity to a greater degree than resistance training without BFR, and this too is a sign of improved cognitive performance. So, in closing, if you struggle with depression, anxiety or stress, I hope you will consider implementing a regular exercise routine as your FIRST line of treatment, rather than your last.

To learn more about KAATSU, join Michael Pupillo's free **KAATSU Q&A Zoom sessions** at the following times and dates (time shown is Pacific Time):

- Mar 14, 2023 09:00 AM
- Mar 16, 2023 09:00 AM
- Mar 21, 2023 09:00 AM
- Mar 23, 2023 09:00 AM
- Mar 28, 2023 09:00 AM

Sources and References

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