High-intensity exercise can reverse neurodegeneration in Parkinson's, study suggests

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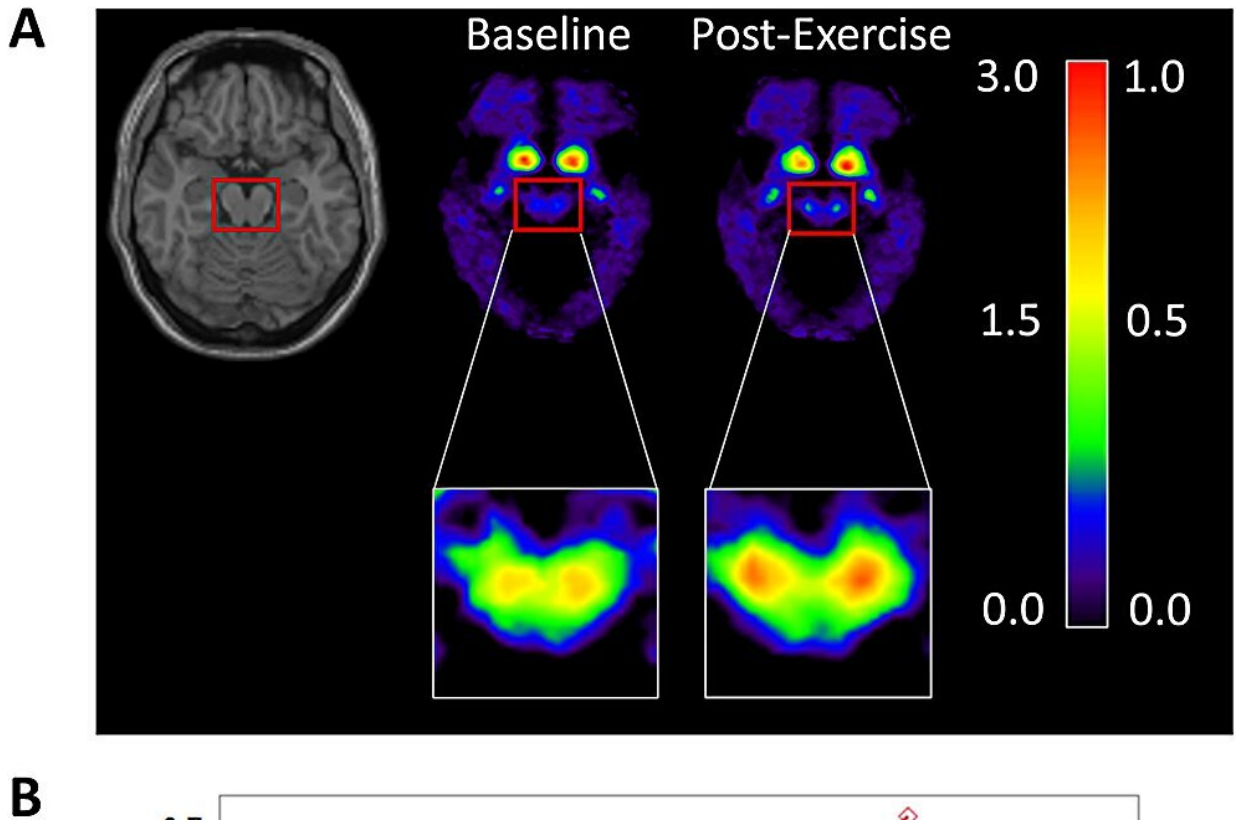

Dopamine Transporter Levels Pre- and Post-Exercise. **A** Average ^{18}F-FE-PE2I DAT BP_{ND} images before and after six months of exercise. The red box including the midbrain and SN is enlarged. **B** ^{18}F-FE-PE2I BP_{ND} in the SN pre- and post-exercise by study participant. Individual lines are red if an increase was observed, blue if a decrease was observed. The solid black line represents the mean of our cohort, the dashed black line represents the expected decrease from

the pre-exercise average in the absence of intervention. Credit: *npj Parkinson's Disease* (2024). DOI: 10.1038/s41531-024-00641-1

High-intensity exercise induces brain-protective effects that have the potential to not just slow down but possibly reverse the neurodegeneration associated with Parkinson's disease, a new pilot study suggests.

Prior research has shown that many forms of exercise are linked to improved symptoms of Parkinson's disease. But there has been no evidence that hitting the gym could create changes at the brain level. Now, a small proof-of-concept study involving 10 patients showed that high-intensity aerobic exercise preserved dopamine-producing neurons, the brain cells that are most vulnerable to destruction in patients with the disease.

In fact, after six months of exercise, the neurons actually had grown healthier and produced stronger dopamine signals. Dopamine is a chemical that helps brain cells communicate with one another. The researchers published their findings in *npj Parkinson's Disease* on February 9.

"This is the first time imaging has been used to confirm that the biology of the brain in those suffering with Parkinson's disease is changed by intense exercise," says Evan D. Morris, Ph.D., professor of radiology and biomedical imaging at Yale School of Medicine and co-principal investigator of the paper.

What causes Parkinson's disease?

Parkinson's disease is a neurodegenerative disorder caused by the

misfolding of alpha synuclein protein that is naturally present in our cells. The misfolded protein accumulates within neurons and damages them.

The dopamine-producing cells that are most affected reside in the part of the brain known as the substantia nigra, an area near the base of the brain. As these cells die off, the lack of dopamine creates the physical symptoms of the disease, particularly motor symptoms such as tremors and slowed movement. It's a gradual progression, and at the time of diagnosis, typically patients have already lost over half of their dopamine-producing neurons.

"By the time patients clinically manifest the typical motor symptoms of Parkinson's, you can assume that the neurodegenerative process actually started much earlier, maybe a decade or two," says Sule Tinaz, MD, Ph.D., associate professor of neurology and co-principal investigator.

The most common available medication, levodopa, replaces the missing dopamine. While the drug is effective in alleviating motor symptoms, it does not prevent the ongoing neurodegeneration and can cause undesirable side effects with long-term use such as uncontrolled excessive movements [dyskinesia]. There is currently no cure for the disease.

Exercise plays a vital role in treating Parkinson's disease

Exercise is an essential component of Parkinson's disease management. In fact, some gyms offer exercise programs specifically for the condition. "I always tell patients that exercise is a part of their treatment," says Tinaz. "The same way I prescribe medication, I also prescribe exercise."

In Connecticut, Michelle Hespeler is the founder of Beat Parkinson's Today, an evidence-based non-profit exercise program that offers online and in-person classes throughout the state. Hespeler was inspired to create her program after being diagnosed with the disease herself. "She took all of the elements of high-intensity interval training and combined it with the needs of people with Parkinson's disease," says Tinaz.

Previously, two well-designed clinical trials have shown that engaging in high-intensity exercise—in which participants reach around 80% to 85% of their age-appropriate maximum heart rate—three times a week for six months is correlated with less severe motor symptoms. "These trials suggested that exercise really is disease-modifying in a clinical sense," says Tinaz. The Yale team used these clinical trials as a model for its new study.

Using brain imaging to study impact of high-intensity exercise

For their study, the Yale researchers recruited patients who had been diagnosed with Parkinson's disease for less than four years. At this early stage of their disease, the patients had not yet lost all of their dopamine-producing neurons. All participants initially went through a two-week trial period to ensure they could handle the intensity of the exercise classes before enrolling.

After the trial period, the participants received their first round of brain scans. One was an MRI scan that measured the amount of neuromelanin—a dark pigment found in dopamine-producing neurons—in the substantia nigra. The second scan was a PET scan that measured dopamine transporter (DAT) availability. DAT is a protein that helps the neurons maintain proper dopamine levels.

Ten participants completed a six-month high-intensity exercise program through Hespeler's Beat Parkinson's Today program. Due to the COVID-19 pandemic, the classes took place online. These classes involve High Intensity Functional Intervals [HIFI] designed to keep participants' heart rates elevated for the majority of the workout. Participants wore heart rate monitors to ensure they were reaching their target heart rates and other wearables (e.g., a Fitbit) to record their movements. After the six months, the researchers repeated the MRI and PET scans.

High-intensity exercise reverses neurodegeneration

Following the six-month program, brain imaging showed a significant increase in both the neuromelanin and DAT signals in the substantia nigra. This suggests that high-intensity exercise not only slowed down the neurodegenerative process, but also helped the dopaminergic system grow healthier.

"Where we would have ordinarily expected to see a decline in the DAT and neuromelanin signals, we saw an increase," says Bart de Laat, Ph.D., associate professor adjunct in psychiatry and the study's first author. "We had hoped to see that the neurodegeneration would not progress as quickly or stop temporarily, but instead we saw an increase in 9 out of 10 people. That was remarkable."

The study highlights the importance of including an exercise regimen as part of one's Parkinson's treatment plan. "The medications we have available are only for symptomatic treatment. They do not change the disease course," says Tinaz. "But exercise seems to go one step beyond and protect the brain at the neuronal level."

While this is an exciting finding, additional research will be needed to fully understand the neuroprotective effects of exercise. The team hopes

that its work will inspire other scientists to prioritize research into exercise and its disease-modifying potential.

Parkinson's disease is the fastest-growing neurological disease. By 2040, researchers estimate that over 12 million people worldwide will be living with the condition. The new study holds promise that exercise can help mitigate the enormous personal and economic costs the disease poses. "Exercise is accessible to everyone, is relatively cheap, and is safe [if your health care provider approves]," says Tinaz. "If it also has this neuroprotective effect with the potential to reverse the disease course, that is something to celebrate and to study."

More information: Bart de Laat et al, Intense exercise increases dopamine transporter and neuromelanin concentrations in the substantia nigra in Parkinson's disease, *npj Parkinson's Disease* (2024). DOI: 10.1038/s41531-024-00641-1

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