Study provides evidence that breathing exercises may reduce Alzheimer's risk

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The exercise was simple: inhale for a count of five, then exhale for a count of five. Do that for 20 minutes, twice a day, for four weeks.

These brief breathing sessions had significant impacts: Volunteers' heart rate variability increased during each exercise period and the levels of amyloid-beta peptides circulating in their blood decreased over the four weeks of the experiment.

That's the finding of a new study from USC Leonard Davis School of Gerontology Professor Mara Mather. Published last month in the journal *Scientific Reports*, the study may be the first to discover a way that adults, both young and old, can reduce their amyloid beta levels: via breathing exercises that lower the levels in our blood of these peptides associated with Alzheimer's disease.

That's because the way we breathe affects our heart rate, which in turn affects our nervous system and the way our brain produces proteins and clears them away. While we are awake and active, we typically use our sympathetic nervous system. This is sometimes known as the "fight or flight" system but we also use it to exercise, to focus attention, and even to help create long-lasting memories. While the sympathetic nervous system is activated, there isn't much variation in the time between each heartbeat. In contrast, when the parasympathetic system is activated, heart rates increase during inhaling and decrease during exhaling.

When we're young—or older, but very fit—our body slides easily between the sympathetic nervous system and its partner, the parasympathetic nervous system. Sometimes known as the "rest and digest" part of our system, the parasympathetic nervous system allows us to calm down, digest food easily, and sleep soundly. When these kinds of activities occur, the variation between heartbeats is greater.

But as we age, scientists are learning, our ability to access our parasympathetic nervous system—and thus, our heart rate variation—decreases dramatically.

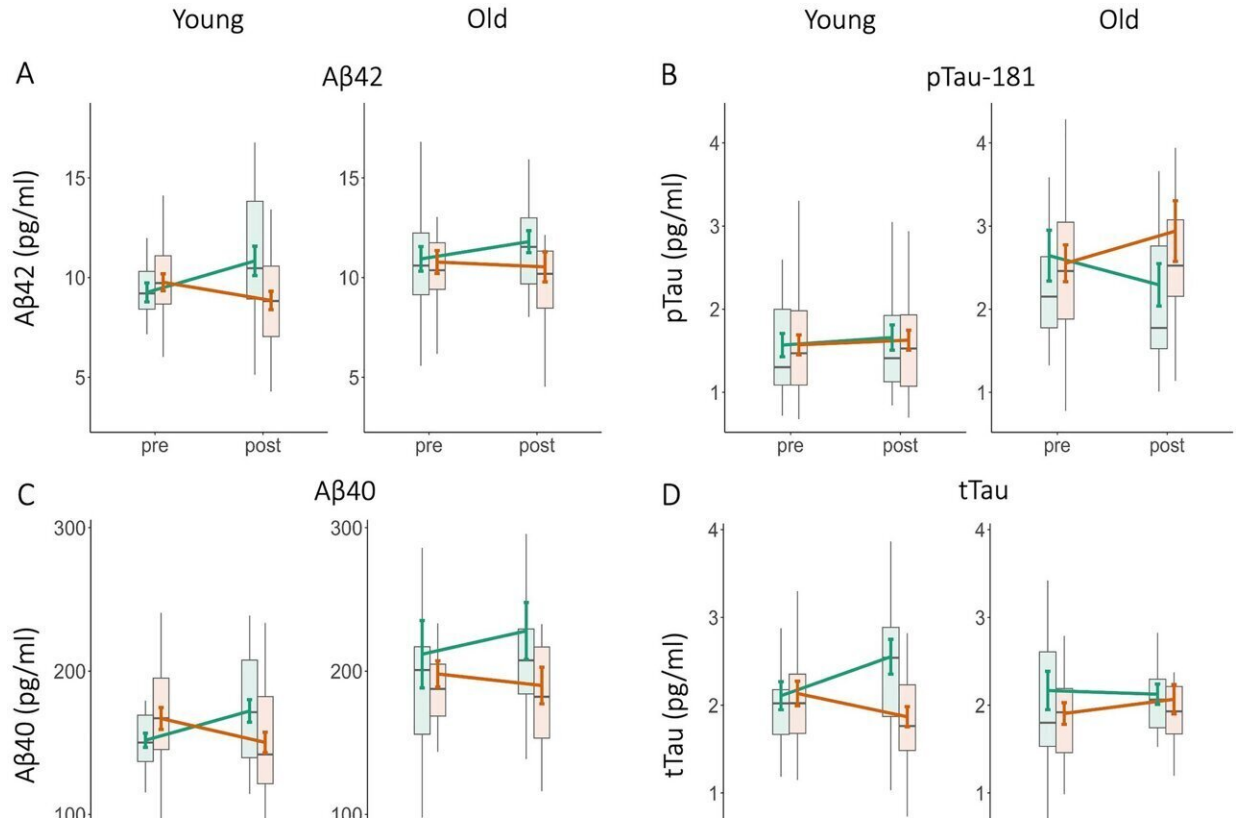
A 2020 study using smart watches found that heart rate variability drops on average 80 percent between twenty and sixty years old. This finding could partially explain why we struggle to sleep deeply as we age.

"We know the sympathetic and parasympathetic systems influence the production and clearance of Alzheimer's related peptides and proteins," said Mather, who directs the Emotion & Cognition Lab at the Leonard Davis School of Gerontology. "Nevertheless, there's been very little research on how these physiological changes in aging might be contributing to the factors that make it conducive for someone to develop Alzheimer's disease or not."

Mather and fellow researchers from USC, UC Irvine and UCLA asked participants to do biofeedback exercises twice a day, for 20 minutes at a time. All the participants clipped a heart monitor onto their ear; that monitor was connected to a laptop the researchers provided.

Half the group was instructed to think of calm things, like a beach scene or a walk in a park, or to listen to calm music. Meanwhile, they were instructed to keep an eye on their heart rate as displayed on the laptop screen, making sure the heart rate line stayed as steady as possible while they meditated.

The other group was told to pace their breathing in rhythm with a pacer on the laptop screen—when the square rose, they inhaled, and when the square dropped, they exhaled. They also monitored their heart rates, which tended to rise in peaks as they inhaled and dip down to baseline as they exhaled. Their goal was to increase the breathing-induced oscillations in their heart rate.



Intervention effect on Aβ and tau levels. Orange represents Osc+ and green represents Osc−. The upper and lower box boundaries indicate the 75th and 25th percentiles respectively. The gray horizontal bar inside each box shows a median value for the box, and the colored vertical line describes the mean and standard error. The outliers are included for the summary statistics but are not shown in the figure. Credit: *Scientific Reports* (2023). DOI: 10.1038/s41598-023-30167-0

The researchers took blood samples before the participants began the experiment and again, after four weeks of biofeedback training. Then the researchers examined the plasma of participants from both groups, looking for amyloid beta peptides.

In particular, the researchers looked at two peptides, amyloid beta 40 and 42.

Accumulation of amyloid beta in the brain due to increased production and/or decreased clearance is believed to trigger the Alzheimer's disease process. In healthy adults who do not yet have signs of amyloid accumulation in the brain, a meta-analysis shows that higher levels of amyloid beta 40 and 42 in circulating blood predicts a greater risk of developing Alzheimer's.

In Mather and colleagues' study, plasma levels of both peptides decreased in the group who breathed slowly and tried to increase their heart rate variability (HRV) by increasing oscillations.

Now researchers want to figure out why the peptides decrease when HRV increases, said Jungwon Min, a graduate student in psychology and the lead author on the study. Is it because fewer peptides are being produced? Or because the body clears them out better? Or some combination of both?

Though the current study does give some hints.

"Based on the data we have, it appears the decrease in amyloid beta is due more to decreased production," she said. "But that doesn't exclude the possibility of increased clearance."

Of the study's 108 participants, half were young (ages 18 to 30) and half were old (ages 55 to 80). The younger and the older adults showed similar effects of the interventions on plasma amyloid beta levels.

The study appears to be the first to find that behavioral interventions can reduce the level of amyloid beta peptides in plasma. Previous research has demonstrated that sleep deprivation and stress can increase amyloid beta levels, but it has proved more challenging to decrease amyloid beta with behavioral interventions.

"At least to date, exercise interventions have not decreased Aβ [amyloid beta] levels," said Mather. "Regularly practicing slow-paced breathing via HRV biofeedback may be a low-cost and low-risk way to reduce plasma Aβ levels and to keep them low throughout adulthood."

Other study co-authors were Kaoru Nashiro, Hyun Joo Yoo, Shai Porat, Christine Cho and Junxiang Wan, of USC; Jeremy Rouanet, Allesandra Cadete Martini, Elizabeth Head, Daniel A. Nation and Julian F. Thayer, of UC Irvine; and Steve W. Cole of UCLA.

More information: Jungwon Min et al, Modulating heart rate oscillation affects plasma amyloid beta and tau levels in younger and older adults, *Scientific Reports* (2023). DOI: 10.1038/s41598-023-30167-0

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