Alzheimer's drug may help maintain mitochondrial function in muscles as it slows cognitive decline

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A common treatment for Alzheimer's disease may help people with the earliest stages of the disease maintain mitochondrial function in their muscles in addition to slowing cognitive decline. The first-of-its-kind study is published ahead of print in *Function*.

Research suggests people with Alzheimer's disease, a form of cognitive impairment, have mitochondrial dysfunction throughout the body. Mitochondria, often described as the "powerhouses of the cells," are the structures inside the cells that produce energy. Previous studies have also shown that people with Alzheimer's disease have reduced exercise capacity compared to healthy adults. However, the mitochondrial function in the muscles of cognitively impaired adults hasn't been studied extensively.

The researchers of a new study investigated adults over the age of 60 who had the earliest stage of Alzheimer's disease-related cognitive decline, called mild cognitive impairment. Some of the participants were not being treated for cognitive impairment, while others were being treated—for at least a month prior to the study—with a medication commonly used to slow the decline of Alzheimer's disease called donepezil. The cognitive impairment groups were compared with a control group of cognitively healthy adults that were matched for age, sex and weight.

The volunteers participated in an exercise test on a treadmill, which measured their exercise capacity. In addition, they were given a fitness tracker to wear at home for seven days. The research team measured the participants' mitochondrial function in their muscles and expression of genes linked to mitochondrial function. The researchers found that the untreated group had reduced mitochondrial function compared to the treated and control groups. Donepezil altered the expression of multiple genes in the treated group, including those involved in mitochondrial regulation and function, fatty acid metabolism and protein synthesis in

the muscles.

"Donepezil significantly reduces the rate of cognitive decline in early [Alzheimer's disease], and our results suggest it may also mediate protection against reductions in skeletal muscle respiratory capacity," the research team wrote. "This work provides additional evidence of systemic mitochondrial dysfunction and muscle metabolism."

Other findings of the study include:

- Volunteers with treated mild cognitive impairment were not as physically active as the untreated and control groups.
- Volunteers with treated mild cognitive impairment tired more quickly during the graded exercise test than the untreated and control groups.
- Volunteers with untreated mild cognitive impairment had less fat mass than the treated and control groups.

More information: Jill K Morris et al, Mild cognitive impairment and donepezil impact mitochondrial respiratory capacity in skeletal muscle, *Function* (2021). DOI: 10.1093/function/zqab045

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