

GlyNAC improves multiple defects in aging to boost strength and cognition in older humans

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A pilot human clinical trial conducted by researchers at Baylor College of Medicine reveals that supplementation with GlyNAC—a combination

of glycine and N-acetylcysteine as precursors of the natural antioxidant glutathione—could improve many age-associated defects in older humans to improve muscle strength and cognition, and promote healthy aging.

Published in the journal *Clinical and Translational Medicine*, the results of this study show that older humans taking GlyNAC for 24 weeks saw improvements in many characteristic defects of aging, including glutathione deficiency, [oxidative stress](#), [mitochondrial dysfunction](#), inflammation, insulin resistance, endothelial dysfunction, body fat, genomic toxicity, [muscle strength](#), gait speed, exercise capacity and cognitive function. The benefits declined after stopping supplementation for 12 weeks. GlyNAC supplementation was well tolerated during the study period.

"There is limited understanding as to why these defects occur in older humans, and effective interventions to reverse these defects are currently limited or lacking," said corresponding author endocrinologist Dr. Rajagopal Sekhar, associate professor of medicine in the Section of Endocrinology, Diabetes and Metabolism at Baylor.

For the last 20 years, Sekhar and his team have been studying natural aging in older humans and aged mice. Their work brings mitochondria, known as the batteries of the cell, as well as free radicals and glutathione to the table in discussions about why we age.

Mitochondrial dysfunction and aging

Mitochondria generate energy needed for supporting cellular functions by burning fat and sugar from foods, therefore mitochondrial health is critically important for life. Sekhar believes that improving the health of malfunctioning mitochondria in aging is the key.

As mitochondria generate energy, they produce waste products such as free radicals. These highly reactive molecules can damage cells, membranes, lipids, proteins and DNA. Cells depend on antioxidants, such as glutathione, the most abundant antioxidant in our cells, to neutralize these toxic free radicals. Failing to neutralize free radicals leads to harmful and damaging oxidative stress that can affect mitochondrial function.

Interestingly, glutathione levels in older people are much lower than those in younger people, and the levels of oxidative stress are much higher.

Animal studies conducted in the Sekhar lab have shown that restoring glutathione levels by providing GlyNAC reverses glutathione deficiency, reduces oxidative stress and fully restores mitochondrial function in aged mice.

"In previous work we showed that supplementing HIV patients with GlyNAC improved multiple deficits associated with premature aging observed in those patients," Sekhar said. "In this study, we wanted to understand the effects of GlyNAC supplementation on many age-associated defects in [older adults](#)."

GlyNAC improves several hallmark defects in aging

The world population of older humans is rapidly increasing and with it comes an increase in many age-related illnesses. To understand what causes unhealthy aging, scientific research has identified nine hallmark defects which are believed to contribute to the aging process.

"It is believed that correcting these aging hallmarks could improve or reverse many age-related disorders and help people age in a healthier way," Sekhar said. "However, we do not fully understand why these

hallmark defects happen, and there are currently no solutions to fix even a single hallmark [defect](#) in aging."

This is where Sekhar's trial results become encouraging, because GlyNAC supplementation for 24 weeks appears to improve four of the nine aging hallmark defects.

To further understand whether GlyNAC holds the keys to mitochondrial recovery and more, Sekhar and his team conducted this pilot clinical trial.

"We worked with eight older adults 70 to 80 years of age, comparing them with gender-matched younger adults between 21 and 30 years old," Sekhar said. "We measured glutathione in red-blood cells, mitochondrial fuel-oxidation, plasma biomarkers of oxidative stress and oxidant damage, inflammation, endothelial function, glucose and insulin, gait-speed, muscle strength, exercise capacity, cognitive tests, gene-damage, glucose-production and muscle-protein breakdown rates and body composition. Before taking GlyNAC, all these measurements were abnormal in older adults when compared with those in younger people."

The older participants took GlyNAC for 24 weeks, and then stopped it for 12 weeks. Sekhar and his colleagues repeated the above measurements at the halfway point at 12 weeks, after 24 weeks of taking GlyNAC, and again after stopping GlyNAC for 12 weeks.

"We are very excited by the results," Sekhar said. "After taking GlyNAC for 24 weeks, all these defects in older adults improved and some reversed to the levels found in young adults." The researchers also determined that older adults tolerated GlyNAC well for 24 weeks. The benefits, however, declined after stopping GlyNAC supplementation for 12 weeks.

"I am particularly encouraged by the improvements in cognition and muscle strength," Sekhar said. "Alzheimer's disease and mild cognitive impairment (MCI) are serious medical conditions affecting memory in older people and leading to dementia, and there are no effective solutions for these disorders. We are exploring the possibility that GlyNAC could help with these conditions by conducting two pilot randomized clinical trials to test whether GlyNAC supplementation could improve defects linked to cognitive decline in Alzheimer's disease and in MCI, and possibly improve cognitive function."

"The overall findings of the current study are highly encouraging," Sekhar said. "They suggest that GlyNAC supplementation could be a simple and viable method to promote and improve healthy aging in older adults. We call this the 'Power of 3' because we believe that it takes the combined benefits of glycine, NAC and glutathione to reach this far reaching and widespread improvement. We also have completed a randomized clinical trial on supplementing GlyNAC vs. placebo in older adults and those results will be forthcoming soon."

More information: Premranjan Kumar et al, Glycine and N-acetylcysteine (GlyNAC) supplementation in older adults improves glutathione deficiency, oxidative stress, mitochondrial dysfunction, inflammation, insulin resistance, endothelial dysfunction, genotoxicity, muscle strength, and cognition: Results of a pilot clinical trial, *Clinical and Translational Medicine* (2021). [DOI: 10.1002/ctm2.372](https://doi.org/10.1002/ctm2.372)

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