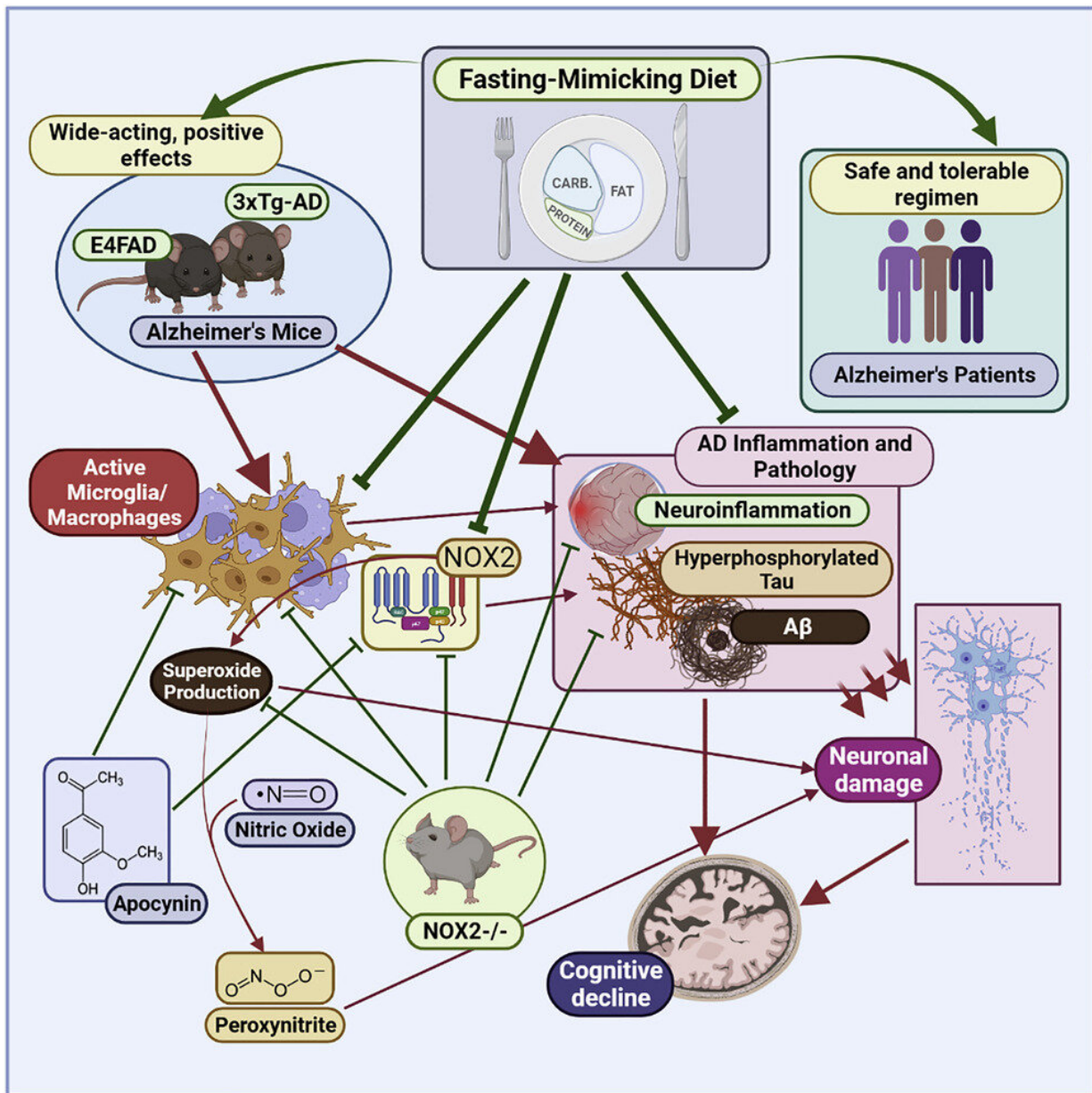


# Fasting-mimicking diet reduces signs of dementia in mice

September 27 2022, by Beth Newcomb



Graphical abstract. Credit: *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111417

Cycles of a diet that mimics fasting appear to reduce signs of Alzheimer's in mice genetically engineered to develop the illness, according to a new USC Leonard Davis School of Gerontology-led study.

The study appeared in *Cell Reports* on Sept. 27.

The researchers, led by Professor Valter Longo in collaboration with Professors Christian Pike and Pinchas Cohen, found that mice that had undergone several cycles of the fasting-mimicking diet showed less Alzheimer's pathology. The researchers found lower levels of two major hallmarks of the disease: amyloid beta—the primary driver of plaque buildup in the brain—and hyperphosphorylated tau protein, which forms tangles in the brain. They also found that brain inflammation lessened and better performance on [cognitive tests](#) compared to the mice that were fed a standard diet.

The fasting-mimicking diet (FMD) is high in [unsaturated fats](#) and low in overall calories, protein, and carbohydrates and is designed to mimic the effects of a water-only fast while still providing necessary nutrients. Previous research led by Longo has indicated that brief, periodic FMD cycles are associated with a range of beneficial effects, including the promotion of [stem cell regeneration](#), lessening of [chemotherapy side effects](#), and [lowering risk factors](#) for cancer, diabetes, [heart disease](#) and other age-related diseases in mice and humans.

## **Promising results in mouse models of Alzheimer's**

Alongside healthy mice, the team investigated two mouse models of Alzheimer's, E4FAD and 3xTg. During the study, mice were fed the fasting-mimicking diet for 4 or 5 days twice per month and were allowed to eat normally between FMD cycles. In a long-term experiment to see the effects in aged mice, 3xTg mice were placed on the diet for 30 cycles in 15 months. Shorter-term experiments in both 3xTg and E4FAD mice ranged from a single FMD cycle to 12 cycles in 6 months.

In both models, mice who underwent FMD cycles showed promising reductions in [amyloid beta](#)—which form the sticky, disruptive plaques in the brain—and tau pathology compared to mice eating a standard diet. The FMD mice also showed lower levels of brain inflammation, including a reduction in the number of active microglia, the immune cells that seek and destroy pathogens and damaged cells in the brain. In addition, mice on the diet demonstrated a lower level of oxidative stress, which plays a role in Alzheimer's pathology by damaging neurons and contributing to the accumulation of amyloid in the brain. The study specifically pointed to the free radical "superoxide" as a central culprit in the damage occurring in these Alzheimer's mouse models, Longo explained.

Outwardly, mice of both Alzheimer's models who underwent the FMD showed less cognitive decline than their standard diet counterparts. Cognitive behavior, including exploration and performance within mazes, was tested in young mice before the dietary regimen began and again after several months of either a [standard diet](#) or twice-monthly FMD cycles. The Alzheimer's mice given the FMD significantly outperformed the Alzheimer's mice given standard diets and in some instances performed similarly to the non-Alzheimer's-prone control mice, indicating that [cognitive decline](#) had been significantly slowed.

The FMD cycles appeared effective in reversing a range of pathology markers but also cognitive defects in two of the major mouse models for

Alzheimer's disease. Longo said that the results are promising.

## Small clinical study explores feasibility for humans

In addition to the study in [mice](#), Longo and colleagues also included data from a small Phase 1 clinical trial of the fasting-mimicking diet in [human patients](#) diagnosed with [mild cognitive impairment](#) or mild Alzheimer's disease. Forty such patients who were otherwise healthy and had family support were randomized to either a once-monthly, 5-day fasting-mimicking diet or a 5-day period in which lunch or dinner was replaced with a meal based on pasta or rice.

Initial data indicates that the FMD is safe and feasible for patients with mild impairment or early Alzheimer's disease. Further tests in the ongoing clinical trial will measure cognitive performance, inflammation and more, Longo said.

Other early trials of the [diet](#) published by Longo and colleagues have indicated other benefits of a monthly cycle, such as a loss of fat mass without loss of muscle mass and improved cardiometabolic risk factors, especially in overweight or obese people.

Notably, in a [recently published clinical trial](#) in which Longo was a co-author, FMD cycles were associated with disease regression in diabetes patients. Diabetes nearly doubles the risk of developing Alzheimer's disease, per the Alzheimer's Association.

**More information:** Priya Rangan et al, Fasting-mimicking diet cycles reduce neuroinflammation to attenuate cognitive decline in Alzheimer's models, *Cell Reports* (2022). [DOI: 10.1016/j.celrep.2022.111417](https://doi.org/10.1016/j.celrep.2022.111417)

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