



Intermittent Fasting for Brain Health

Intermittent fasting and calorie restriction induce the process of autophagy, the cellular self-cleansing process that rids cells of junk. Autophagy notably declines with age, leading to a decreased ability to clear damage, and since aging just is an increase in damage, the decline in autophagy leads to even more damage in a vicious cycle.

The decline in autophagy has implications for the brain, as brain disorders like Alzheimer's are characterized by increased amounts of junk molecules, such as beta amyloid and lipofuscin. [1. Hardy, John, and Dennis J. Selkoe. "The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics." *Science* 297.5580 (2002): 353-356.]

Fasting and brain function

Could intermittent fasting help protect against a decline in brain function? Yes, it could.

Consider that a drug that induces autophagy is neuroprotective and decreased the accumulation of misfolded, junk proteins.[2. Tsvetkov, Andrey S., et al. "A small-molecule scaffold induces autophagy in primary neurons and protects against toxicity in a Huntington disease model." *Proceedings of the National Academy of Sciences* 107.39 (2010): 16982-16987.]

But we can get the same or similar results without a drug.

Short-term fasting induces profound neuronal autophagy.[3. Alirezaei, Mehrdad, et al. "Short-term fasting induces profound neuronal autophagy." *Autophagy* 6.6 (2010): 702-710.]

Disruption of autophagy—a key homeostatic process in which

cytosolic components are degraded and recycled through lysosomes—can cause neurodegeneration in tissue culture and in vivo. Up-regulation of this pathway may be neuroprotective, and much effort is being invested in developing drugs that cross the blood brain barrier and increase neuronal autophagy. One well-recognized way of inducing autophagy is by food restriction, which up-regulates autophagy in many organs including the liver; but current dogma holds that the brain escapes this effect, perhaps because it is a metabolically-privileged site. **...we show that short-term fasting leads to a dramatic up-regulation in neuronal autophagy... Our data lead us to speculate that sporadic fasting might represent a simple, safe and inexpensive means to promote this potentially-therapeutic neuronal response.**

How does this work? The answer is simple: in the absence of food, the body needs certain constituents to maintain normal function. For energy, it breaks down fat – obviously, since you lose fat when you don't eat.

The body also requires amino acids, the constituents of protein molecules. Autophagy breaks down proteins to supply amino acids, and in something of a miracle of biological function, it preferentially selects misfolded and non-functional proteins for destruction.

Hence increasing autophagy through fasting leads to better brain health.[4. Anson, R. Michael, et al. "Intermittent fasting dissociates beneficial effects of dietary restriction on glucose metabolism and neuronal resistance to injury from calorie intake." *Proceedings of the National Academy of Sciences* 100.10 (2003): 6216-6220.]

Ghrelin, the hunger hormone

A recent study found that the hormone ghrelin stimulates autophagy in neurons (brain cells).[5. Ferreira-Marques, Marisa, et al. "Caloric restriction stimulates autophagy in rat cortical neurons through neuropeptide Y and ghrelin receptors activation." *Aging* 8.7 (2016).]

Ghrelin is known as the hunger hormone and has a central role in the regulation of feeding.[6. Nakazato, Masamitsu, et al. "A role for ghrelin in the central regulation of feeding." *Nature* 409.6817 (2001): 194-198.]

This all makes sense: fasting stimulates hunger through the increase in ghrelin, which in turn stimulates autophagy.

Another implication of the role of ghrelin in hunger and autophagy is that if you actually feel hungry, your autophagy rate has likely gone way up – a good thing. So if you get hungry while fasting, just realize that you're promoting a very healthful process in your body – not to mention the promotion of fat loss.

Insulin, fasting, and autophagy

It turns out that other hormones are important to stimulating autophagy too. A group investigating a cell-culture model of autophagy found that omitting a certain supplemental nutrient formula from the culture potently induced autophagy.[7. Young, Jessica E., Refugio A. Martinez, and Albert R. La Spada. "Nutrient deprivation induces neuronal autophagy and implicates reduced insulin signaling in neuroprotective autophagy activation." *Journal of Biological Chemistry* 284.4 (2009): 2363-2373.]

By a process of elimination, they discovered that the absence of one ingredient in the cell-culture supplement caused a large increase in autophagy, and that ingredient was the hormone insulin.

Insulin is produced in response to carbohydrates and protein in food. (Ingestion of fat causes little or no increase in insulin.) [Fasting produces a potent and swift drop in insulin levels.](#)

In our era of high-carb food and 24/7 food availability, most people's insulin levels never drop much, leading to insulin resistance and obesity. They never go long enough without food, especially carbohydrates, to see much of a drop in insulin.

This has implications for aging. [Eating all the time](#) will accelerate the aging process.

The brains of overweight people show much more shrinkage and are functionally ten years older than the brains of lean people.[8. <https://www.cam.ac.uk/research/news/brains-of-overweight-people-ten-years-older-than-lean-counterparts-at-middle-age>]

This could be due to inflammation caused by excess fat tissue, or through insulin levels that are always high, or some other mechanism(s).

Fasting at least some of the time is necessary for good brain health and slowing the aging process.

My speculation is that even someone who fasts only 12 hours a day, i.e. between dinner and breakfast, would have a dramatically lower chance of brain disorders. These days, most people don't do that.

You could greatly increase brain health by fasting longer, such as 16 hours or more, say from dinner until lunchtime the next day. Or longer, even 24 hours or more.

Conclusion

- Autophagy declines with age, leading to accumulation of junk in the neurons of the brain
- Increased junk is implicated in brain disorders like Alzheimer's
- Fasting strongly increases autophagy in neurons
- Both the presence of ghrelin and the absence of insulin are implicated

in increased autophagy

- Fasting regularly will improve brain health and lessen the risk of cognitive decline and brain disorders

PS: [Check out my Supplements Buying Guide for Men.](#) Intermittent fasting is an integral part of my anti-aging program in my book, [Stop the Clock.](#)