Fasting

A Six-Part Series and Getting Started Guide

Craig Constantine

This collection brings together a six-part series exploring the science of fasting alongside a practical guide to getting started with 16:8 intermittent fasting.

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by Craig Constantine

Introduction

This collection brings together a six-part series exploring the science of fasting alongside a practical guide to getting started with 16:8 intermittent fasting.

The series begins by questioning long-held assumptions about meal timing and examines what actually happens in the body during a fast — from the metabolic switch to fat burning, through autophagy and cellular repair, to hormonal changes, immune renewal, and the neurological effects that fasting practitioners often report as mental clarity. Each installment weighs the research honestly, distinguishing strong evidence from speculation and noting where the science is still catching up to the claims. The final piece shifts from understanding to doing, offering a stepped approach to building a 16-hour fasting practice, drawing on personal experience rather than theory.

I've been doing 16:8 intermittent fasting for years and recently started 48-hour fasts — dropping about three pounds each fast, gaining one or two back, and trending steadily downward. I wanted to understand what the research actually says about what I'm doing to myself, so I worked with Claude (Anthropic's AI) to produce this series. I set the structure, chose the topics, pushed back on claims that felt hand-wavy, and guided the editorial tone. Claude did the writing and research synthesis. My curiosity driving Claude's research and prose.

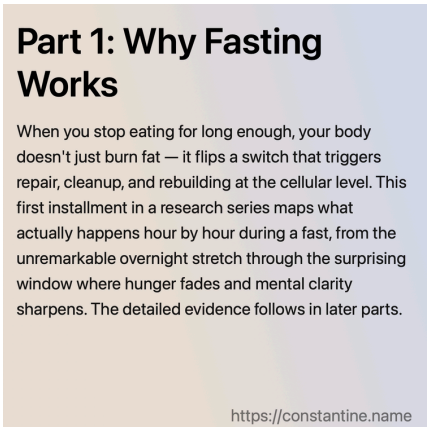
These posts were originally published on my blog at constantine.name, where you can find these and other posts about fasting.

Part 1: Why Fasting Works →

March 4, 2026

The Big Picture

Research brief — general overview of fasting benefits. The most "hand-wavy" of the series: frameworks, history, and the broad case for why not eating is doing something useful.



The Metabolic Switch

The overarching framework for understanding fasting benefits comes from Mark Mattson's "metabolic switch" concept, reviewed comprehensively in a landmark 2019 NEJM paper co-authored with Rafael de Cabo. (1)

The core idea: when you stop eating for long enough, the body shifts from glucose-based to ketone-based energy. This isn't just a fuel swap — it's a stress response that activates adaptive cellular pathways. The metabolic stress of fasting triggers increased expression of antioxidant defenses, DNA repair, protein quality control, mitochondrial biogenesis, and autophagy. These protective mechanisms outlast the fast itself — a hormetic effect where controlled stress leaves the system stronger.

This is the thread that connects the individual benefits explored in the rest of this series: better insulin sensitivity, growth hormone surges, inflammation reduction, cellular cleanup, and (possibly) neurological benefits all flow from this same metabolic switch.

The Breakfast Myth — How We Got Here

Before talking about what fasting does, it's worth understanding what we were told about *not* fasting — specifically, the idea that skipping breakfast is harmful.

"Breakfast is the most important meal of the day" is not a scientific finding. It's a marketing slogan.

The history: A 1944 marketing campaign by General Foods (maker of Grape Nuts) distributed

pamphlets in grocery stores and ran radio ads declaring that "Nutrition experts say breakfast is the most important meal of the day." (2) Some sources trace the phrase further back to a 1917 article in a magazine published by John Harvey Kellogg's Battle Creek Sanitarium. (3, 4) The cereal industry systematically funded and promoted research that supported breakfast eating, creating a self-reinforcing cycle of industry-funded studies and marketing claims. Harvard nutrition professor Dr. David Ludwig has stated that the idea breakfast is essential comes from the food industry's historical push, not from unbiased research.

Note on the Bernays connection: Edward Bernays (the "father of PR") is often credited with creating the "bacon and eggs" breakfast campaign in the 1920s, working for Beech-Nut Packing Company. This is a separate but parallel story — Bernays promoted a *hearty* breakfast; the "most important meal" language appears to come from the cereal companies. The two threads are often conflated online.

What the science actually shows: A 2019 BMJ meta-analysis by Sievert et al. at Monash University examined 13 RCTs on breakfast and weight. Breakfast skippers had a small weight advantage (mean difference 0.44 kg), and breakfast eaters consumed ~260 more calories per day. Adding breakfast did not improve weight loss regardless of whether participants were habitual breakfast eaters or skippers. (5)

Quality caveat the authors themselves flag: all included trials were at high or unclear risk of bias with short follow-ups (mean 7 weeks for weight, 2 weeks for energy intake).

The adults vs. children distinction: The observational evidence for breakfast benefiting children and adolescents — particularly for cognitive performance and academic outcomes — is stronger than for adults. Growing brains may be more sensitive to glucose availability after overnight fasting. But adults have larger glycogen reserves, better metabolic flexibility, and less acute sensitivity to short-term fuel gaps. The honest framing: the evidence that breakfast matters may hold for growing children, but for adults, the "most important meal" claim was born in a marketing department and has not been substantiated by rigorous research.

So: skip breakfast. For adults, it's not the mythological "most important meal" — it's the easiest meal to drop, and dropping it is one of the simplest onramps to intermittent fasting (see Part 2).

What Happens When You Don't Eat

A rough timeline of what the body does during a fast, painting in broad strokes (the details and evidence for each are in Parts 3–6):

- **0–12 hours:** The body works through available glucose and glycogen stores. Insulin drops. Nothing dramatic yet — this is a normal overnight fast.
- **12–18 hours:** Glycogen depletes. The liver begins producing ketone bodies. Fat mobilization accelerates. You're entering mild ketosis.
- **18–24 hours:** Ketone levels rise. Growth hormone begins increasing. Autophagy pathways are activating. Inflammatory monocytes start clearing from circulation.
- **24–48 hours:** Full ketosis. Growth hormone surging (up to 5-fold by 48 hours). Autophagy well underway. Insulin at baseline. The "keto flu" window — electrolyte shifts can cause headache, fatigue, brain fog — typically peaks here and resolves as the brain adapts to ketone fuel.
- **48–72 hours:** Deep into the fasting response. Stem cell priming begins (per Longo's research). Many people report hunger *diminishing* rather than intensifying. Mental clarity often peaks as the brain runs efficiently on ketones.
- **Refeeding:** The regenerative burst. Stem cells that were primed during the fast activate. The system rebuilds from a cleaner baseline.

This timeline is approximate and draws from both human and animal data. The specific evidence behind each claim — including where it's strong and where it's hand-wavy — is covered in the subsequent parts.

Sources

1. de Cabo & Mattson 2019, *NEJM* — effects of IF on health, aging, and disease: https://pubmed.ncbi.nlm.nih.gov/31881139/ (full text paywalled: https://www.nejm.org/doi/full/10.1056/NEJMra1905136)
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5. Sievert et al. 2019, *BMJ* — breakfast and weight/energy intake meta-analysis: https://pubmed.ncbi.nlm.nih.gov/30700403/ (free full text: https://pmc.ncbi.nlm.nih.gov/articles/PMC6352874/)

Part 2: Getting Into Fasting →

March 4, 2026

Routines, Scenarios, and What to Expect

Research brief — the practical onramp. 16:8 IF as a starting point, Craig's specific eating window, extended fasting scenarios anchored to a weekly rhythm, and what keto flu actually is.

Start With 16:8

You may want to start by getting into 16:8 intermittent fasting — an 8-hour eating window and 16-hour fast — before attempting anything longer.

Is this actually supported? Honestly, no one has studied whether practicing 16:8 first makes longer fasts easier. It's conventional wisdom without a clinical trial behind it. But the physiological rationale is sound: regular time-restricted eating develops **metabolic flexibility** — the ability to switch between glucose and fat/ketone oxidation. Someone who does this daily would be expected to enter ketosis faster and with less discomfort during an extended fast. And the practical experience of managing hunger, learning your body's signals, and knowing what electrolyte depletion feels like are real benefits of prior fasting experience, even if unstudied. (1)

What the research says about 16:8 on its own:

Satchin Panda's group at the Salk Institute pioneered time-restricted eating (TRE) research, starting with a 2012 mouse study that showed mice on a high-fat diet restricted to an 8-hour eating window didn't gain weight compared to ad libitum fed mice eating the same food. (2) Human trials with 6–10 hour eating windows have generally shown weight loss, improved glucose regulation, reduced hunger, and improved energy.

A 2020 study by Wilkinson et al. put 19 participants with metabolic syndrome on a 10-hour eating window for 12 weeks and found reductions in weight, blood pressure, and atherogenic lipids. Single-arm trial (no control group), but notable results. (3)

The Eating Window: Skip Breakfast

The simplest way to do 16:8 is to skip breakfast. Eat your first meal around 11:30 AM, finish eating by 7:30 PM. That's it.

Example daily rhythm:

- **11:30 AM** — First meal ("break fast")
- **2:00–3:00 PM** — Protein-heavy snack if hungry (0% fat yogurt, protein shake with fruit)
- **5:30–6:00 PM** — Dinner
- **Nothing after 7:30 PM**

This gives you a clean 16-hour overnight fast every day. No special foods, no supplements, no elaborate protocols. Just… don't eat in the morning.

But isn't an earlier window better? Courtney Peterson's group published the first controlled feeding trial of early time-restricted feeding (eTRF) in 2018. Men with prediabetes ate within a 6-hour window ending at 3 PM vs. a 12-hour window. eTRF improved insulin sensitivity, blood pressure, oxidative stress, and appetite — **even without weight loss**. (4)

Peterson's data suggests an earlier window (say, 8 AM–4 PM) may have slightly better metabolic outcomes due to circadian alignment — insulin sensitivity and glucose tolerance are naturally higher in the morning. But the practical reality is that most people can't eat their last meal at 3 PM. Social eating, family dinners, real life — the later window is far more sustainable. Peterson's data shows early TRE is *better*, not that late TRE is *bad*. An 11:30–7:30 window still captures the core benefits of a compressed eating window and extended overnight fast.

Extended Fasting Scenarios

Once 16:8 feels routine, you can extend into longer fasts. All scenarios below are anchored to a Sunday ~5:30 PM family meal as the break-fast, working backward:

- ~22 hrs — Saturday dinner (7:30 PM) Extended one-meal-a-day. Easy entry point beyond 16:8.
- ~30 hrs — Saturday lunch (11:30 AM) Skip one full day of eating. You sleep through the hardest part.
- ~46 hrs — Friday dinner (7:30 PM) Nearly two full days. Well into ketosis and autophagy is active. Two sleeps make this more manageable than it sounds.
- ~54 hrs — Friday lunch (11:30 AM) Deep into the autophagy/stem cell priming window. Friday afternoon might be the grittiest stretch — you're still burning through glucose stores

and haven't hit the ketone clarity yet.

- ~70 hrs — Thursday dinner (7:30 PM) Three full days. Firmly in Longo's regenerative territory. Most people report hunger actually *diminishing* after day 2.
- ~78 hrs — Thursday lunch (11:30 AM) The "long weekend fast." Maximizes time in the 48–72+ hour zone where stem cell and deep autophagy research is strongest.

I've recently been fasting in the 46-hour to 54-hour options to hit a sweet spot — you get the major benefits (see Parts 3–6), Sunday dinner is a natural social re-entry, and you're only navigating one or two workdays while fasting. The jump from 54 to 70+ is where most people feel they're making a real lifestyle commitment for the week rather than a weekend experiment.

Keto Flu: What It Is and Why It Happens

Sometime in the 24–72 hour window, you'll likely hit the "keto flu" — headache, fatigue, brain fog, irritability, maybe muscle cramps. It actually feels a bit like you're coming down with the flu. It's not illness. It's electrolytes. When I stop eating around Noon on Friday, this happens (if I don't address the underlying cause beforehand) in the middle of the night Saturday.

Here's the mechanism:

1. **Insulin drops** — your kidneys stop retaining sodium and excrete more water. (Insulin normally signals the kidneys to reabsorb sodium.)
2. **SGLT2 effect:** The sodium-glucose transport protein 2 normally reabsorbs glucose and sodium together in a 1:1 ratio. With blood glucose low, SGLT2 activity drops, and more sodium goes out in your urine.
3. **Sodium loss drags potassium and magnesium** along with it through coupled renal transport.
4. The resulting electrolyte imbalance — particularly sodium depletion — drives the entire symptom cluster.

This is well-established physiology, not speculative. (5)

The mental fog typically lifts as the brain adapts to using ketones for fuel. Many people describe a shift to unusual mental clarity once adaptation kicks in — probably related to the brain's efficient use of beta-hydroxybutyrate (BHB) as fuel.

For me, Friday afternoon until bed is the grittiest stretch on a 46–54 hour fast; By Saturday midday I feel exceptionally sharp.

Sources

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Part 3: Cellular Cleanup →

March 4, 2026

Autophagy

Research brief — what autophagy is, what the evidence actually shows, and where the common claims outrun the science.

What Autophagy Is

Autophagy — from Greek *auto* ("self") and *phagein* ("to eat") — is the process by which cells degrade and recycle damaged organelles, misfolded proteins, and dysfunctional mitochondria. Think of it as cellular housekeeping: damaged parts get broken down and the raw materials get repurposed for repair and new construction.

Yoshinori Ohsumi won the 2016 Nobel Prize in Physiology or Medicine for discovering the genetic

mechanisms of autophagy. Working in baker's yeast in the early 1990s, he identified the genes essential for the process. The mechanisms are highly conserved across species including humans. (1)

The molecular trigger is well-understood: nutrient deprivation suppresses insulin and mTOR signaling and activates AMPK — all of which are upstream regulators of autophagy. The logical chain from "fasting — reduced insulin/mTOR — autophagy activation" is mechanistically solid. Disrupted autophagy has been linked to Parkinson's disease, type 2 diabetes, Alzheimer's, certain cancers, and many infections. (2)

What We Don't Know in Humans

This is where the common claims outrun the evidence. Most of what people confidently state about fasting and autophagy in humans is extrapolated from animal models.

The measurement problem: You can't biopsy someone's liver or brain during a fast to count autophagosomes. The available approaches in living humans:

- **Peripheral blood mononuclear cells (PBMCs):** Researchers measure the LC3B-II/LC3B-I ratio in blood cells treated with chloroquine ex vivo. This is an indirect proxy — it tells you something is happening in immune cells, not necessarily what's happening in liver, muscle, or brain tissue.
- **LC3 and p62/SQSTM1 in tissue biopsies:** More direct but rarely done in fasting studies on healthy humans because it requires invasive sampling.
- **Interpretation challenge:** Elevated LC3 levels can reflect either *enhanced* autophagy or *impaired* autophagic flux (a blocked process, not an active one). The marker alone doesn't tell you which.

A registered clinical trial (NCT04842864) titled "Time Course for Fasting-induced Autophagy in Humans" exists on ClinicalTrials.gov — the fact that this is still an active research question tells you something about how unsettled the timing is. (3)

A 2022 study by Chaudhary et al. found that intermittent fasting activated markers of autophagy in mouse liver but **not** in muscle from either mice or humans. Tissue-specific responses mean blanket claims about "autophagy ramping up everywhere at 24 hours" are oversimplified. (4)

What Can Be Said Honestly

The commonly cited "autophagy kicks in at 24–48 hours" is a reasonable estimate based on animal data and indirect human markers, not a precisely measured human threshold. The molecular

machinery is real. The upstream triggers (low insulin, low mTOR, active AMPK) are clearly activated during a 48-hour fast. A 48-hour fast almost certainly activates autophagy in at least some human tissues. But "how much" and "exactly when" are not precisely known in humans, and the response varies by tissue type.

The metabolic switch framework (Part 1) places autophagy activation as one of several adaptive cellular stress responses triggered by the shift from glucose to ketone metabolism. (5) It doesn't happen in isolation — it's part of a broader cascade that includes DNA repair, protein quality control, and mitochondrial biogenesis.

Evidence strength: Moderate. Mechanism is solid. Direct human measurement is thin. The claim that autophagy is active during a 48-hour fast is well-supported mechanistically but not precisely quantified in humans.

Sources

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Part 4: Hormonal Shifts →

March 4, 2026

Growth Hormone and Insulin Sensitivity

Research brief — the two best-evidenced hormonal responses to extended fasting, with direct human measurements.

Growth Hormone Surge

Human growth hormone (HGH) secretion increases substantially during fasting. This is among the best-measured effects of fasting in humans — researchers have drawn blood every 5 minutes over 24-hour periods to capture the pulsatile secretion patterns.

Ho et al. 1988 — Examined 24-hour GH secretion patterns in six normal adult men during fed and fasting states (day 1 and day 5 of a 5-day fast). Found that fasting enhances GH secretion through both increased pulse frequency and amplitude. (1)

Hartman et al. 1992 — The definitive study. Nine normal men, blood sampling every 5 minutes over 24 hours. Found a *-fold increase in 24-hour endogenous GH production during a two-day fast, mediated by increased secretory burst frequency and amplitude. Notably, IGF-1 concentrations were unchanged after 56 hours of fasting. (2)

The 5-fold figure from Hartman is the basis for the commonly cited “2–5x increase” claim. The range exists because individual responses vary and different studies measure slightly different things (peak amplitude vs. 24-hour integrated production).

What this does: The GH surge during fasting supports lean tissue preservation and fat mobilization. The body is shifting from burning glucose to burning fat, and elevated GH helps protect muscle mass during this transition while directing the body to use fat stores as fuel. This is part of the metabolic switch (Part 1) — the body isn’t just passively running out of food, it’s actively reconfiguring which tissues to protect and which fuel sources to tap.

Caveats: Both studies used small samples of healthy men (6 and 9 participants respectively). The findings are consistent with each other and with the broader endocrinology literature, but most subjects were young-to-middle-aged males. The GH response to fasting in women and older

adults is less thoroughly characterized, though directionally similar results have been observed.

Evidence strength: Strong. Direct human measurements, replicated findings, published in top endocrinology journals. Small sample sizes but consistent results.

Insulin Sensitivity

Fasting for 48 hours produces a dramatic drop in circulating insulin and measurable improvement in insulin sensitivity. This is one of the most robustly demonstrated effects of extended fasting in human studies.

The mechanism is straightforward: with no incoming glucose, the body needs less insulin. Insulin levels drop to baseline. Cells that have been chronically exposed to high insulin (and have down-regulated their insulin receptors in response) get a reset. When food is reintroduced, the cells respond to insulin more readily.

The de Cabo & Mattson 2019 NEJM review covers this comprehensively, describing how intermittent fasting triggers neuroendocrine responses characterized by low levels of amino acids, glucose, and insulin. Eating within a 6-hour period and fasting for 18 hours can trigger the metabolic switch, with measurable improvements in insulin sensitivity. (3)

This isn't subtle or contested — it's one of the clearest, most directly measured effects of fasting. It's also one of the most practically relevant for the large portion of the population dealing with insulin resistance, prediabetes, or metabolic syndrome.

Connection to 16:8 (Part 2): Even daily time-restricted eating improves insulin sensitivity. Sutton et al. 2018 showed that early TRE improved insulin sensitivity in men with prediabetes **even without weight loss** — the time restriction alone was enough. (4) Extended fasts amplify this effect further.

Evidence strength: Strong. Multiple human studies, reviewed in a major journal, physiologically straightforward.

Sources

1. Ho et al. 1988, *J Clin Invest*, 81(4):968-75 — fasting enhances GH secretion: https://pubmed.ncbi.nlm.nih.gov/3127426/ (free full text: https://pmc.ncbi.nlm.nih.gov/articles/PMC329619/)

2. Hartman et al. 1992, *J Clin Endocrinol Metab*, 74(4):757-65 — 5-fold GH increase during 2-day fast: https://pubmed.ncbi.nlm.nih.gov/1548337/
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Part 5: Inflammation and Immune Renewal →

March 4, 2026

Inflammation and Immune Renewal

Research brief — how fasting reduces systemic inflammation and primes the immune system for regeneration. Two distinct but related mechanisms.

Inflammation Reduction

Jordan et al. 2019 — Stefan Jordan, Navpreet Tung, and colleagues at the Icahn School of Medicine at Mount Sinai, led by Miriam Merad. Published in *Cell*, 178:1102-1114. (1)

This study directly tied caloric intake to the circulating inflammatory monocyte pool — a key driver of systemic inflammation.

What they found:

- Short-term fasting reduced monocyte metabolic and inflammatory activity and drastically reduced the number of circulating monocytes
- The mechanism: fasting activates AMPK in hepatocytes (liver cells) and suppresses systemic CCL2 production via PPARα, which reduces monocyte mobilization from bone mar-

row
- Fasting improved chronic inflammatory diseases *without* compromising emergency immune mobilization during acute infection — the immune system's ability to respond to real threats remained intact

The human component: The study profiled 12 healthy, normal-weight volunteers at 3 hours post-meal and at 19 hours fasting. The mouse experiments used longer fasting periods and showed more dramatic effects.

Caveat: The human fasting window studied was 19 hours, not 48. The mouse data showed more dramatic effects with longer fasts. Extrapolating to 48 hours is directionally reasonable — if 19 hours produces measurable monocyte reduction, 48 hours would be expected to produce more — but the specific magnitude at 48 hours in humans was not tested in this study.

This connects to the metabolic switch framework (Part 1): the drop in insulin and shift to ketone metabolism activates the same AMPK pathway that suppresses inflammatory monocyte mobilization. It also connects to autophagy (Part 3) — the cellular cleanup machinery is part of the same adaptive stress response.

Evidence strength: Strong for the mechanism, moderate for the specific 48-hour timepoint in humans.

Stem Cell Priming and Immune Regeneration

Cheng et al. 2014 — Chia-Wei Cheng, Gregor B. Adams, Valter D. Longo and colleagues at USC. Published in *Cell Stem Cell*, 14(6):810-23. (2)

This is the Longo lab study that generated the "fasting regenerates the immune system" headlines. The reality is more nuanced but still remarkable.

What they found:

- Prolonged fasting (48–72 hours in mice; fasting-mimicking diet cycles in humans) reduces circulating IGF-1 and PKA activity
- This promotes hematopoietic stem cell (HSC) self-renewal and lineage-balanced regeneration
- Multiple cycles of fasting reversed age-dependent myeloid bias in mice — essentially resetting the immune system's tendency to produce more inflammatory cells as it ages
- Multiple fasting cycles reduced immunosuppression and mortality caused by chemotherapy
- Preliminary human data showed protection of lymphocytes from chemotoxicity during fast-

ing

The refeeding insight: The regenerative benefit largely manifests during **refeeding**, not during the fast itself. The fast *primes* the stem cells by reducing IGF-1 and PKA signaling; the refeeding phase *triggers* the regenerative burst. This is often omitted in popular accounts — people focus on what happens during the fast, but the rebuild happens when you eat again. This makes the break-fast meal (Sunday dinner in the scenarios from Part 2) more than just the end of the fast — it's the beginning of the regenerative phase.

Important caveats:

- The 48–72 hour window comes from mouse data
- The human component of this study used fasting-mimicking diet (FMD) cycles, not water fasting
- The human data was preliminary — Longo's subsequent work has focused more on FMD than on water fasting per se
- The pro-regenerative effects were demonstrated after *multiple cycles* of fasting, not a single fast

Connection to the 46–54 hour fasting scenarios (Part 2): A 46-hour fast (Friday dinner to Sunday dinner) puts you at the lower edge of the window where this research becomes relevant. A 54-hour fast (Friday lunch to Sunday dinner) is solidly in the range. The 70–78 hour options maximize time in this territory.

Evidence strength: Strong in mice, preliminary in humans. The 48–72 hour window is from animal models. The refeeding-as-regeneration finding is well-supported.

Sources

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Part 6: The Brain →

March 4, 2026

Mental Clarity, BDNF, and Ketone Fuel

Research brief — what happens in the brain during extended fasting. The subjective experience of mental clarity is real and widely reported; the science behind it is more complicated than the popular narrative suggests.

The Clarity People Report

Many people describe a distinct shift during extended fasting — typically somewhere after the 24–36 hour mark — from brain fog to unusual mental clarity. This is one of the most consistently reported subjective experiences of fasting, across cultures and contexts. It's real. The question is why.

Three candidate explanations, not mutually exclusive:

1. **Ketone metabolism** — the brain runs efficiently on beta-hydroxybutyrate (BHB)
2. **BDNF upregulation** — fasting may increase brain-derived neurotrophic factor
3. **Stable fuel supply** — no more blood sugar fluctuations from meals

The first and third have strong physiological grounding. The second is where the science gets shaky.

Ketones as Brain Fuel

By 48 hours of fasting, the liver is producing ketone bodies — primarily BHB — as the body's main fuel source. The brain, which normally relies heavily on glucose, can use BHB efficiently. Some researchers argue the brain actually runs *more* efficiently on ketones than on glucose in certain contexts, producing more ATP per unit of oxygen consumed.

This is part of the metabolic switch described in Part 1. (1) The shift from glucose to ketone-based energy isn't just happening in muscles and liver — the brain is making the same transition, and the subjective experience of clarity likely tracks with this fuel switch completing. The "keto flu" brain fog (Part 2) happens during the messy transition; the clarity arrives once the brain has fully adapted to the new fuel source.

Evidence strength: Strong. The biochemistry of ketone metabolism in the brain is well-established.

BDNF — The Overhyped Claim

Brain-derived neurotrophic factor (BDNF) supports neuroplasticity, neuronal resilience, and the growth of new synaptic connections. Animal studies consistently show that fasting upregulates BDNF, which is why it's frequently cited as a fasting benefit.

The human picture is much murkier.

A 2024 systematic review published in *Medicina* examined 16 human studies (from 2000–2023) on intermittent fasting, calorie restriction, and BDNF levels. The results were strikingly split: (2)

- 5 studies showed significant BDNF **increase** after fasting interventions
- 5 studies showed significant BDNF **decrease**
- 6 studies showed **no significant change**

That's about as close to "we don't know" as a systematic review can get. The review concluded that IF has "varying effects on BDNF levels" in humans.

A 2022 narrative review in *Frontiers in Aging* attempted to synthesize the neurotrophic effects of IF, calorie restriction, and exercise, and similarly found the human BDNF evidence to be inconsistent and insufficient for strong conclusions. (3)

Why the disconnect between animal and human data? Several possibilities:

- Animal studies typically measure BDNF in brain tissue directly; human studies rely on blood BDNF levels, which may not reflect what's happening in the brain
- The fasting protocols studied in humans vary enormously (Ramadan fasting, alternate-day fasting, calorie restriction, time-restricted eating) — these may not all trigger the same neurological responses
- Measurement timing matters — when in the fasting/refeeding cycle you measure BDNF may produce different results

Honest assessment: The subjective mental clarity during extended fasts is real. Attributing it specifically to BDNF upregulation in humans is not supported by the current evidence. The more likely drivers are ketone metabolism (well-established) and the absence of postprandial blood sugar fluctuations (straightforward physiology).

Evidence strength: Strong in animals, weak and contradictory in humans. This is the weakest of the claimed fasting benefits in this series.

The Stable Fuel Supply

This is the simplest explanation and possibly the most underrated: when you're not eating, your blood sugar isn't spiking and crashing. The brain receives a steady supply of ketones instead of riding the glucose roller coaster. For anyone who normally experiences afternoon energy dips, post-meal drowsiness, or reactive hypoglycemia, the stable fuel supply of ketosis may account for much of the perceived clarity — not through some exotic neurotrophic mechanism, but simply by removing the disruptions.

Evidence strength: Physiologically obvious but rarely studied in isolation because it's hard to disentangle from the other effects of fasting.

Sources

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Getting started with 16-hour fasting →

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This post is about ways to incrementally change when you are eating, to shift yourself from how you are eating today, to a particular time-pattern of fasting called 16:8 (pronounced “sixteen eight”.) 16:8 means every day you have a 16-hour fast (the “not eating” window,) and then an 8-hour eating window.

I’m going to start by assuming you already want to begin fasting. I’ve written more generally about fasting if you’d prefer to start with WHY you might want to try being more intentional about when you choose to eat.

Putting yourself into “intentional” mode

You SHOULD discuss your fasting with your primary care physician. Ask them what you should be aware of, or how it may affect you—they know the specifics of your body. You will discover they actually know all about fasting and diet. If you are proactively engaged in your own welfare, your physician will be happy to be a font of useful information.

For example: My primary care doctor is well aware of the beneficial effects of diet, exercise and fasting on my cholesterol markers. They are also convinced that my lifestyle changes will not be able to *sufficiently* improve those markers *quickly enough.* Thus, our discussions and my choices continue.

(And—yikes!—if your physician isn’t helpful, knowledgeable, and open to discussion, you should find a better physician.)

Fasting is about WHEN you eat

Fasting is easy to understand: It’s about WHEN you eat. Whether we use the word fasting, intermittent fasting (IF), or time restricted eating (TRE), we’re simply referring to when you eat versus when you don’t eat.

Fasting—here, and whenever I talk about it—is not about depriving yourself, nor about starvation or suffering. It is SIMPLY being intentional about WHEN you CHOOSE to eat.

I know, I know… 16 hours without eating probably sounds like a crazy-long time to not eat. But as I said at the top, I'm assuming you are motivated to try this.

Breakfast versus break-fast

Important nuance in my writing: "breakfast" versus "break-fast".

The meal we call breakfast got its name because it is breaking your overnight fast. See, you've been doing intermittent fasting, daily your entire life, every night! Then every morning you break your fast at some point. We've simply learned through habituation to *rush* to food upon waking, and so breakfast became that meal we eat early every morning. (Aside: It is not the most important meal.)

I write "breakfast" to refer to an **early morning** break-fast meal.

I write "break-fast" when I simply want to refer to whatever you eat, whenever it is, to break your fast each day. For example, I eat break-fast at 11:30 a.m., often with other people who simply call the meal lunch.

Diet is WHAT you eat

"To go on a diet" somehow turned into "self-deprivation to lose weight." Your diet is simply the entire suite of things you eat. The topic of fasting is separate from the topic of diet. Where there are many reasons to change your diet, this piece only mentions things directly related to fasting.

Let's clarify what "not eating" means: 16-hours is *in reality* a very short time to not eat. The only thing you *actually* need to ingest is water. So not-eating means ingesting just water. That's the easiest way to do it; If it isn't water, then don't put it in your mouth during the fast.

There's a huge amount of discussion about what else you can ingest without losing the *benefits* of fasting—plain teas, black coffee, a pinch of salt in water, perhaps even some broth. But "only water" is simple.

This transition to 16:8 IF is easier if you eliminate some of the added sugar and some carbohydrates from your diet. (Or at least change some of the carbs for lower glycemic index carbs; brown rice for white, whole potatoes for chips or crackers, etc.) High carbohydrate diets create blood sugar swings that manufacture *additional* hunger urges, independent of actual caloric need hunger. The on-ramp to 16:8 and the shift toward lower-carbohydrate (and don't misread that as "low-", or "no-") eating reinforce each other; it's worth doing them together.

From today to 16:8 IF

Most people eating in the Western pattern are running something like a 14- or 15-hour EATING window. So we could say that's 10:14 IF or 9:15 IF. Again you are already fasting every day! But you cannot go from that, to 16:8 IF in one jump without suffering, (or worse, without having actual medical problems.)

Here again: Your physician understands your blood panels and if you enter into a *conversation* about fasting you will be much happier. Rest assured, your body is amazing and with small changes over time it turns out to be easy to get benefits from fasting. I no longer think of how I eat as 16:8 IF—it's simply normal, healthy eating.

(The strange part is how often everyone tries to feed me. Sometimes I feel like a duck being gavaged with grain.)

Step 0: The end goal is to eat between 11:30 a.m. and 7:30 p.m.

This is the eating window which fits best with the usual Western SOCIAL styles and patterns.

You can do lunches (but you'll think of it as break-fast) and dinners with everyone else. No one even has to know you are one of those people who is intentional about WHEN they eat.

Step 1: Pin down the beginning

It turns out that your body will habituate to the TIMES you normally eat. You can move your eating window around every day, but *that* requires willpower to fight your physical hunger sensations. Therefore your goal is to have the same 16:8 times every day. Yes, seven days a week. Obviously, you can make exceptions any time you want. But the definition of "exception" implies that you are *normally* doing something the same every day.

The easiest place to start isn't the morning. "Just skip breakfast" is not at all easy! Breakfast is the meal your BODY is most-conditioned to expect.

The easiest place to start is in the evening.

Pick a hard stop-time for your eating window and stick to it.

You shouldn't be eating close to bed time anyway (and maybe you should also fix your sleep?) Start by daily shifting your eating window "close" time earlier, away from when you go to sleep. I recommend shifting it, then doing that for a few days, then shift again. Do that until you get to "no food after" 7:30 p.m.

Step 2: Decide about caffeine

If you're a plain-tea drinker, you get to entirely skip this step!

Up top, I said "nothing but water." If you're a coffee drinker, you've been sweating (or in denial?) about the idea of giving up your morning coffee. Sorry, but anything you're putting into your coffee breaks your fast. (There is debate about whether or not zero-calorie additives end the benefits of fasting—but why would you put *that* in your coffee?)

You are addicted to, and habituated to expect, the caffeine *and* the sugar and fat in your morning coffee. There I said it.

If you break your sugar addiction and habituated expectation, you will come to *love* your favorite coffees (or teas if you decide to switch.) I shifted to black coffee countless years ago, and now I *lust* after great coffee. There's an entire world of coffee to explore and today you can't taste any of that.

Therefore, I recommend your second step be to transition to black coffee. If you desire (you do not "need" them) the milk and the sugar, then that's a break-fast meal. You'll be moving that meal to later and later each day. You can have any drink you like (e.g., a latte which is half(!) milk and half coffee) with your break-fast meal. My point is simply that since you're addicted to the caffeine, you probably want to keep the caffeine.

At this point you're still eating whatever breakfast is your usual, but you're now having a plain beverage that in itself won't break your fast. In fact, you'll soon be looking forward to that yummy coffee. When we start moving breakfast later, you can use the plain coffee as a willpower prop when the night snacking monster tempts you. "No, thank you, Snack Monster. I'm going to bed soon, and then I get to get up and have my morning coffee." And that coffee won't break your fast.

Step 3: Widen the not-eating window

At this point, you have a comfortable eating-window close time, and you have your caffeine addiction separated from your break-fast. (You're still rushing to eat breakfast though.) Now you can turn your attention to breakfast.

Simply by having a set closing-time for your daily eating window (7:30 p.m.) you're probably already doing a 12 or 13 hour fast every day. That's *already* a huge win. There are real—small, but real— beneficial effects (there's a table of hourly duration effects in there) at this fasting duration.

Your next goal isn't to skip breakfast outright. That tends to feel punishing and creates an adversarial relationship with the whole project. The goal is to make breakfast lighter and later.

Lighter…

A low-carbohydrate first meal, eaten an hour after waking does two things: It avoids spiking insulin first thing in the morning (which triggers a wave of hunger a few hours later when it subsides), and it starts conditioning your body to run comfortably on less. The entire time you're extending the fasting window, your body is up-regulating all the biological processes that enable you to run (for many days, by the way) on stored fat.

This is also the step where you can get creative with your breakfast and start imagining what you might want to eventually have for your break-fast meal. You can *actually* eat anything you desire for your breakfast. You are simply conditioned to eat, whatever it is you think breakfast is supposed to be. This is a great chance to try something else.

Later…

Don't try to move your meal in tiny increments; That's just day after day of feeling hungry and thinking about eating while watching the clock. Instead move breakfast a half hour (at least). That gives you time to do something. When you get the craving to eat, remind yourself what you're doing, then go be busy with something else. The craving to eat will pass. Then eat your breakfast at the time you've chosen. I went so far as to plan, the night before, a few small things that I would do if I felt the urge to eat before the time I intended. ("Ah! I'm hungry… go do that load of laundry.")

Black coffee (or plain tea) is your friend here. It provides pleasantness without breaking your fast. In the very beginning, black coffee was enough to get me through the morning while I was still *thinking* about food. These days, I *love* my morning coffee and there's no urge to eat with my coffee. Depending on what I ate the previous day, sometimes I drink my coffee with others eating their breakfast and the food isn't even tempting; I just love my coffee and the social aspect of the meal.

Step 4: Break-fast at 11:30 a.m.

The last adjustment to reach 16:8 is simply to continue sliding your break-fast later. An hour later this week. Another hour next week. Your hunger signals will adjust — this is not a permanent white-knuckling exercise. After a few weeks your body simply expects food at 11:30 a.m. The hunger that feels so urgent when you started turns out to have been habit, not physiology, and

habits can be changed.

Epilogue

There are complex situations where you may want to be fasted at a specific time of day. You can simply shift your eating window a couple hours every day, until you're having your break-fast after the desired time. There's a limit to how late you can eat break-fast though, because you have to eat enough, in the "eating window" while also getting to sleep. All of which will lead you to schedule fasting-required things before 2 p.m. Or, once 16:8 is normal, you simply skip your usual break-fast for the day you need to be fasted at 3 p.m. You won't even notice that day is a 20-hour fast.

About the Author

Craig Constantine is a guide for intentional living. His background in Aikido taught him consistency and responsibility; discovering Art du Déplacement in his 40s reshaped how he lives and teaches. Everything he creates — podcasts, thousands of blog posts, and tools for reflection — traces back to three words: Discovery. Reflection. Efficacy.

Craig's vision is a world where everyone can flourish. His mission is creating better conversations that spread understanding and compassion. A meaningful life, he writes, isn't chased but rather is noticed, one moment at a time.

Learn more at craigconstantine.com and find all of his fasting posts at constantine.name/tag/fasting.