Anti-Aging Studies Are Seriously Compromised

Valter Longo, the noted scientist in aging research, has published a number of studies about fasting as an anti-aging measure. He's developed a fasting-mimicking diet to be used for extended fasts, which I wrote about here. He and colleagues have a new study out, but the question in my mind now is, does the fasting-mimicking diet work? It may not be as effective as advertised, because anti-aging studies are seriously compromised, including this one.

Extended fasting

Intermittent fasting is the practice of going without food for some period of time. An intermittent fast would usually last a minimum of 16 hours, and extend to 24 hours, perhaps more. Definitions in these matters are not totally arbitrary, but are rather loose. Beyond 24 hours or so, a fast that extends into days, would not be an intermittent fast, but an extended fast.

Previous studies have found anti-aging effects, including immune system regeneration, with extended fasting. Keep in mind that when a mouse or rat is fasted for several days, that's a very long time in human terms.

The current study looked at humans on a fasting-mimicking diet.

Fasting-mimicking diet

Extended fasts of several days can be difficult, if not physically then psychologically, and to get around the difficulty, Longo has developed a fasting-mimicking diet. (Discussed in my previous article.) The idea is that a low-calorie, low-fat, low-protein diet for 5 days will not raise insulin of IGF-1, and thus this diet effectively, or nearly enough, physiologically mimics complete fasting.

The current, just-published study is called "Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease". A layman's summary says:

Fasting: More than a fad

> Mice that fast periodically are healthier, metabolically speaking. To explore whether fasting can help people as well, Wei *et al.* studied 71 people who either consumed a fasting-mimicking diet for 5 days each month for 3 months or maintained their normal diet for 3 months and then switched to the fasting schedule. The fasting-like diet reduced body weight and body fat, lowered blood pressure, and decreased the hormone IGF-1, which has been implicated in aging and disease. A post hoc analysis replicated these results and also showed that fasting decreased BMI, glucose, triglycerides, cholesterol, and C-reactive protein (a marker for inflammation). These effects were generally larger in the subjects who were at greater risk of disease at the start of the study. A larger study is needed to replicate these results, but they raise the possibility that fasting may be a practical road to a healthy metabolic system.

In sum, the participants decreased:

- blood pressure
- body weight and fat
- IGF-1, the growth hormone implicated in aging
- blood glucose
- cholesterol
- triglycerides
- C-reactive protein

However, a significant caveat to the above is that changes in glucose, triglycerides, and C-reactive protein overall were not significant; an analysis revealed that changes occurred only in high-risk participants.

One would have to agree that these results look great, and if so, why do I question whether the diet worked?

The answer lies in the baseline values of the participants.

- Only ~37% were of normal weight, with ~39% being overweight (BMI between 25 and 30), and ~24% being obese (BMI >30). The subjects were on average somewhat leaner than an average group of Americans, but not much.
- Body fat: the paper gives body fat in terms of total volume, but lean body mass in terms of percent; doing a calculation reveals that the average body fat percent was about 34%. Even with the fact that over 60% of the participants were women, that’s a lot. They were fat.
- What did they eat normally? No information is given, but the average American eats 20 teaspoons of sugar daily, and the diet of the average American is 50% carbohydrate.

My point is that the participants who ate the fasting-mimicking diet were fairly typical: they were overweight, had high body fat and low muscle mass, and most likely ate like the typical American with plenty of processed junk.

***Of course* if you drop their calorie intake and they eat less crap food, they're going to have better health markers. That's a given.**

What about people who already eat well, with a carbohydrate percentage well under 50%, with no refined carbs or sugar or vegetable oil, no processed junk food, and who have low body fat and exercise regularly? Is the fasting-mimicking diet going to strongly decelerate your aging?

Not likely.

Calorie restriction may not even work

A similar phenomenon is at work in animal studies of calorie restriction, which is the most robust life-extension intervention known.

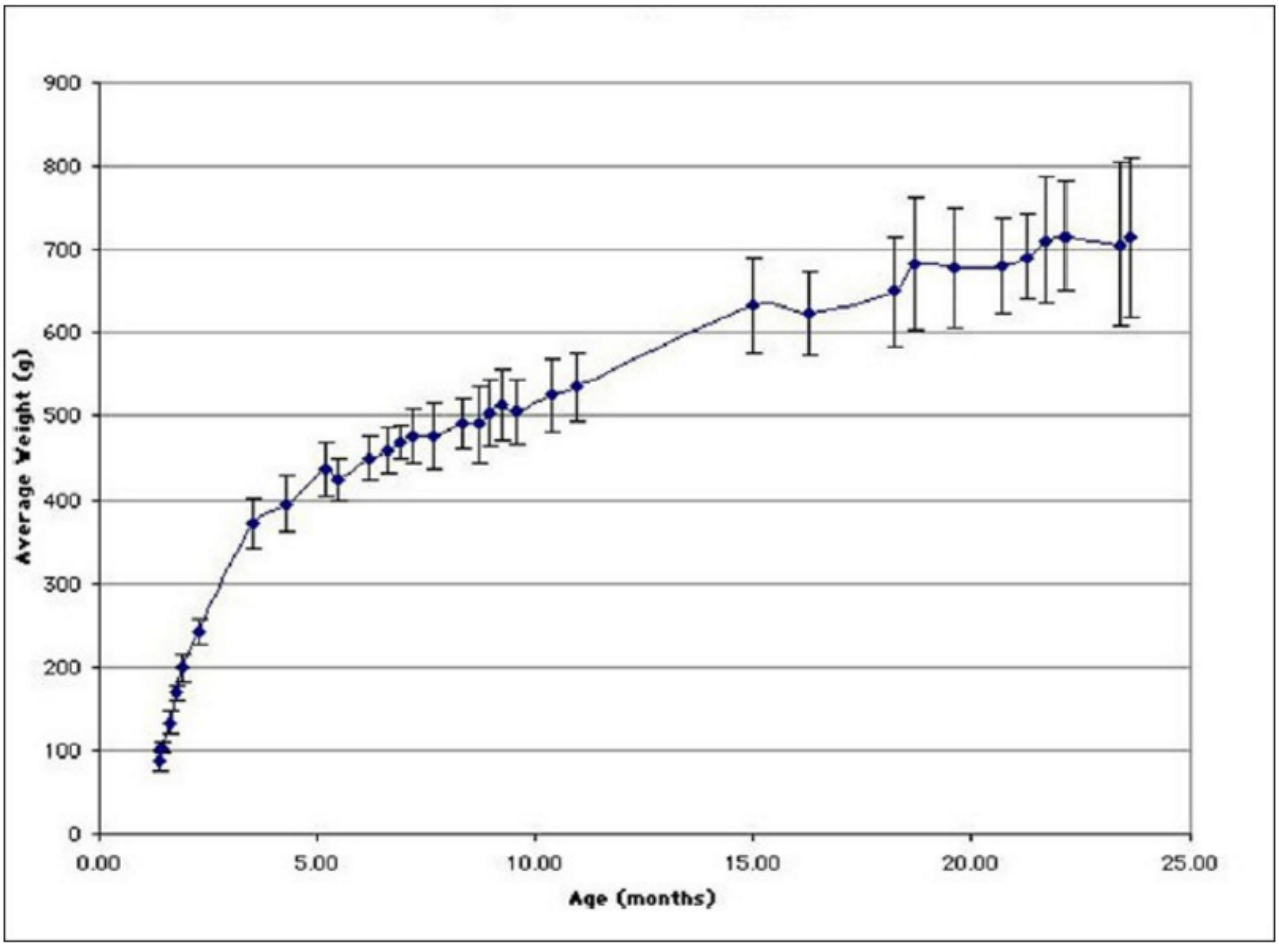
The food that scientists feed lab rats and mice is garbage, loaded with sugar and vegetable oil and toxic amounts of iron. Do you think eating less of that will extend their lives? Not surprisingly, the answer is yes.

Lab mice and rats that are used as controls in calorie restriction studies are metabolically morbid. With their garbage food, and kept in cages with little exercise, the average control rat or mouse becomes obese as they age.

So the question arises: does calorie restriction really extend lifespan by slowing aging, or do the animals just live longer because they don't become obese or develop diabetes?

Calorie restriction does not appear to extend the lifespans of wild mice.

Below is a chart of the weight of (lab) rats throughout their lifespans. (From here.) Rats are fully mature, according to the same article, at 5 to 6 months. Do wild rats gain weight after maturity? That seems doubtful to me, and very old rats, assuming they survived long enough in the wild, would be likely to *lose* weight. But in the laboratory, they gain weight steadily throughout life, and that does not seem normal. They become metabolically morbid and overweight/obese.



Variations in body weight of male rats throughout the lifespan

Any intervention that prevents their weight gain will prolong their lives, but that does not mean it will prolong the lives of normal rats or humans.

Added: In "Impact of caloric restriction on health and survival in rhesus monkeys: the NIA study", the authors discuss why the NIA monkeys did not show an increase in lifespan, while in another study, the WNPRC, they did. Answer: the control animals in WNPRC were fed junk diets with nearly 30% sucrose — yes, you read that right, the control animals got tons of table sugar.

> A notable difference between the two studies is the composition of the monkey diets….
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> Fat content of the NIA study diet was derived from soy oil and the oils from the other natural ingredients (i.e. corn, wheat, and fish). Fish meal contains approximately 8–12% fat and is rich in omega-3 fatty acids. **The WNPRC study dietary fat was derived from corn oil.** [Corn oil is known to promote cancer.] Carbohydrate content was also strikingly different; although both diets have 57–61% carbohydrate by weight, the NIA study diet was comprised primarily of ground wheat and corn, while the WNPRC study diet contained corn starch and sucrose. Indeed, **the WNPRC diet was 28.5% sucrose, while the NIA study diet was only 3.9% sucrose.** This latter point may be particularly important as a diet high in

sucrose can contribute to the incidence of type II diabetes.

Drosophila melanogaster, the fruit fly, is often used in studies of aging. Over a 3-year period of adaptation to laboratory conditions, they undergo a rapid loss of stress resistance. One might look at these as the fly equivalent of obese lab animals or humans. Studying aging in this population will give faulty data.

In my opinion, this is a scandal.

Conclusion: Aging studies need an overhaul

Fasting studies in humans and calorie restriction studies in animals both appear to suffer from control groups that are metabolically morbid. Sick people and animals.

The majority of Americans, about 80%, are not 100% healthy and suffer from chronic health problems to one degree or another. If a diet, a fast, or other regimen corrects some of those problems, that does not mean that it slows aging, only that the participants became less metabolically morbid.

If a calorie restriction regimen extended animals' lives, much of the time that might be only because they were prevented from becoming obese. Wild mice may be living optimally for life extension already, and restricting their food in wild conditions may do nothing. What they need is protection from predators.

What's needed are studies using metabolically healthy humans and animals at baseline, and then finding out whether a given intervention helps them. But good luck with that. Cost and convenience are huge factors in any scientific study. Labs don't want to pay staff to come in to feed animals on weekends, for instance, and they want to use the cheapest, most convenient food.

Lab food contains toxic levels of iron, up to 10 times the requirement, and as animals age, their body iron stores increase dramatically, causing misfolding of proteins and oxidative stress and sarcopenia. Hey, maybe it's the food? I've hammered on this topic, but expect it to go nowhere as usual.

I've lately become much more skeptical about studies in aging, and those are the reasons why.

PS: Here's the talking head version in which I discuss the various fasting and CR experiments and what they mean for the science of aging.

Supplements Buying Guide for Men.

PPS: I was contacted by the new site Geroscience.com and asked for a mention. Looks to be a very worthwhile site dedicated to the science of aging, and written by professionals.