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Transforming Health — How to Navigate Reductive Stress and the Metabolic Impact of Dietary Fats

Analysis by Dr. Joseph Mercola | November 8, 2026

STORY AT-A-GLANCE

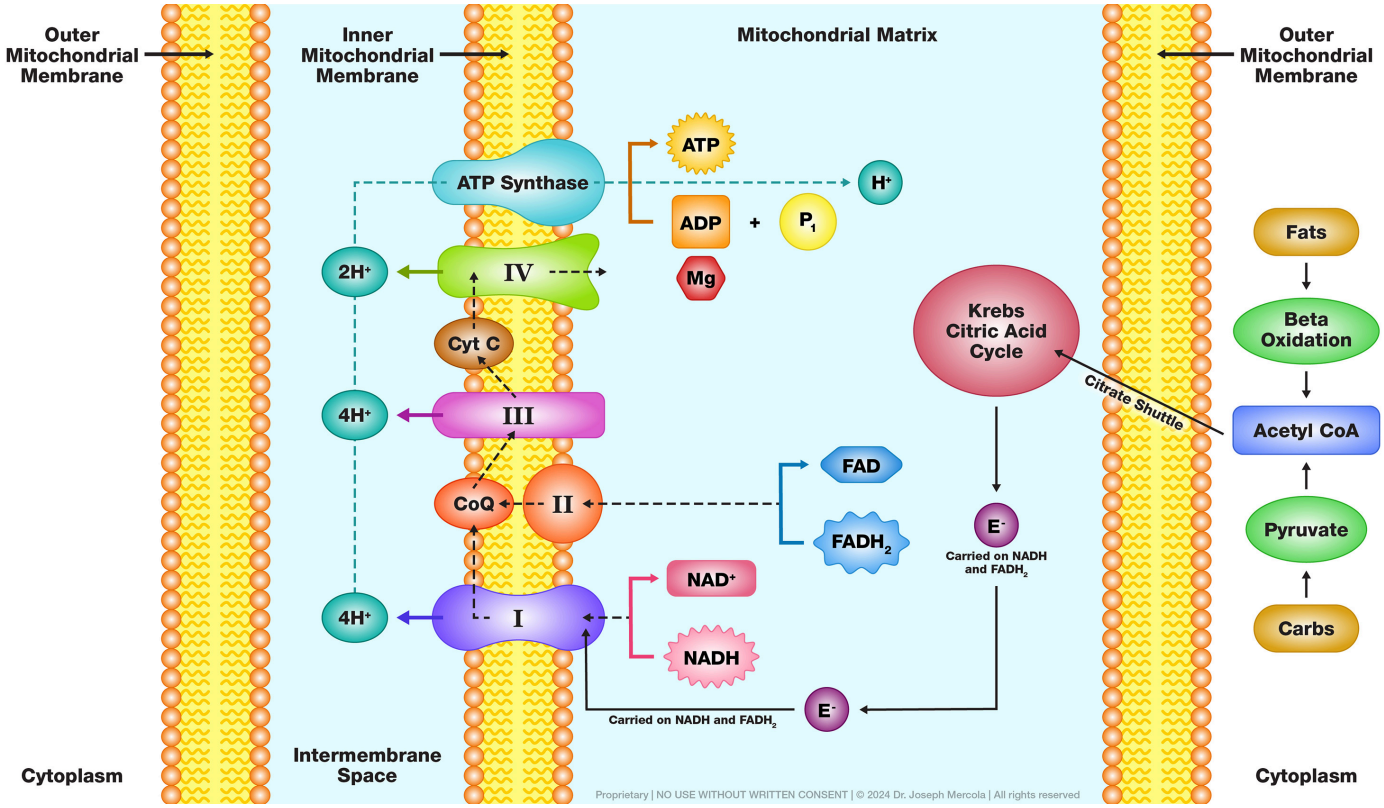
- Reductive stress, caused by an excess of electrons in the electron transport chain, decreases metabolism and may contribute to many degenerative diseases
- Dietary fats, particularly the balance of saturated and unsaturated, have a direct influence on your metabolic rate and health. High consumption of polyunsaturated fats (PUFs) may mimic signals for metabolic slowdown, contributing to metabolic syndrome
- Desaturase enzymes, which are affected by dietary fats, appear to signal your body to adjust its metabolic rate for energy conservation
- Interview guest and Mercola.com research director Brad Marshall links monounsaturated fats (MUFs) like oleic acid to slower metabolic rate and increased reductive stress. Strategies to improve your metabolic health include managing your dietary fat intake
- Marshall also discusses stearoylethanolamide (SEA), a compound made from stearic acid that, in animal research, appears to counter some of the effects of MUFs. Marshall sells his own brand of SEA supplement on his own website

Editor's Note: This article is a reprint. It was originally published May 26, 2024.

In this interview,[1] repeat guest Brad Marshall, a molecular biologist and Mercola.com research director, explains how different dietary fats influence your metabolism and overall health. You may want to listen to this interview a couple of times. If you still find

it hard to understand, copy and paste the corresponding sections of the transcript into ChatGPT and ask it to explain it to you in even simpler terms.

In our previous interview, Marshall explained **reductive stress** and how the damage it causes may contribute to many degenerative diseases and several of the most common causes of death. Molecular biology can be hard to understand which is why I created the best 2-D illustration of how your body creates cellular energy. It will be helpful for you to review this illustration during our discussion.



The other strategy that will help you learn this important information is to have a dialog with ChatGPT or your favorite large language model and ask it to help explain any concepts you don't understand. If the answer is something you still don't understand ask Chat to simplify its answer. Continue asking questions until you understand everything.

In summary, reductive stress results from an excess of electrons that slow down your metabolism and energy production. It's like your body's systems are overwhelmed with energy they can't properly use, which leads to decreased efficiency and damage over time.

Why is it so important to understand these concepts? Because they're the central keys to your health. If you understand these foundational concepts, you can make choices that can help move you away from disease and toward health — because your body wants to be healthy. It's designed to be healthy and is far better able to get there once you give it what it needs.

How Dietary Fats Affect Metabolism

As explained by Marshall, reductive stress and metabolic syndrome might be better understood through the lens of evolution and animal behaviors like torpor — a state of decreased metabolic activity.

Animals adapt by changing the types of fat in their bodies seasonally to prepare for periods of dormancy like hibernation. Marshall argues that one of the signals that triggers this fat composition change is the type of fats consumed in the animal's diet.

For instance, he suggests that eating insects with a high saturated fat content — as tropical ants have been found to have — may have signaled to early mammals the need for a more active metabolism suited to warmer climates. Conversely, diets high in monounsaturated fats (MUFs), like those of ants in colder regions, may signal the approach of winter, prompting animals to lower their metabolic rate in preparation for hibernation.

Key components of this process are desaturase enzymes, which are responsible for adjusting the types of fats within your cells. Examples include Delta-6-desaturase, Delta-5-desaturase, and Delta-9-desaturase — all of which add double bonds to fatty acids. Delta-9-desaturase (also called SCD1) converts saturated fats into MUFs, while delta-6 and delta-5 act on polyunsaturated fats (PUFs).

According to Marshall, ramping up these enzymes appears to signal your body to slow down its metabolic rate in anticipation of periods when less energy will be required or available.

As animals approach colder months, they naturally increase the production of these desaturase enzymes. This increase leads to a higher concentration of MUFs in the body, which is more efficiently stored as fat. This accumulation is part of the body's preparation to conserve energy and maintain survival during periods of scarcity.

Thus, you could say that desaturase enzymes act as a metabolic switch that turns on your body's torpor mode. By modifying the fat composition within your body, they appear to lower your metabolic rate, allowing your body to conserve energy.

And again, this switch is influenced by the type of fat you consume. In mouse research by James Ntambi,[2] saturated fat was linked to a higher metabolic rate and less reductive stress, while feeding the mice a lot of unsaturated fat — MUFs and PUFs — pushed them into reductive stress, which Marshall links to a lower metabolic rate.

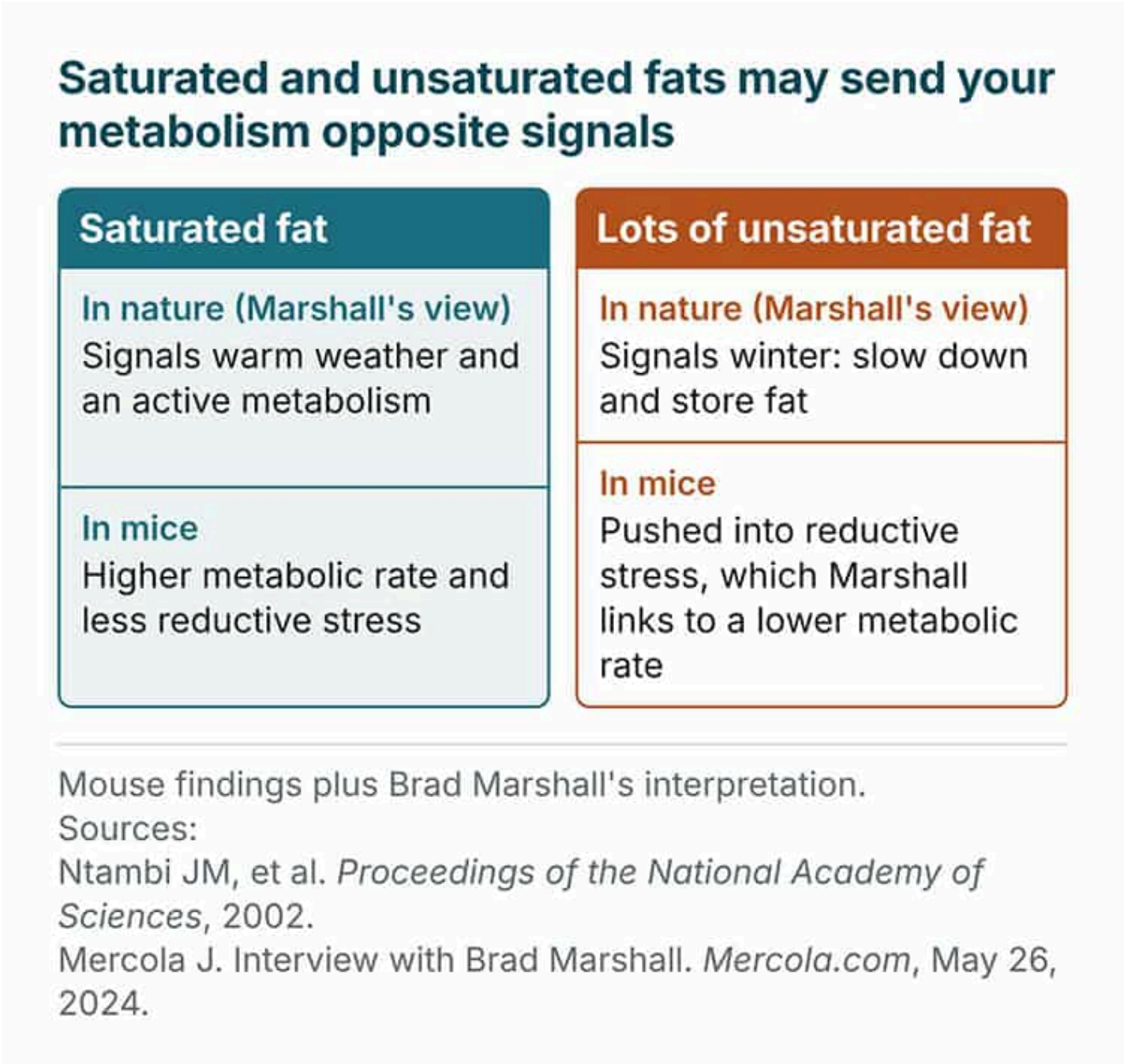


Figure 1. *Saturated fat was linked to a higher metabolic rate in mice, while lots of unsaturated fat pushed them into reductive stress, which Marshall links to a slower, winter-like metabolism.*

In short, if you consume high amounts of PUFs, you may be tricking your body into thinking you need to conserve energy for hard times, like a famine or long winter with scarce food supplies. This process of conservation, in turn, may downregulate or shut down various biological processes because your body doesn't have enough energy for all of them.

Why Linoleic Acid Can Be Metabolically Disruptive

While we typically don't think of torpor applying to humans, Marshall's view is that many Americans may be in a torpor-like state. The increase in unsaturated fats in the human diet over the last century — particularly PUFs — may mimic the natural signal for animals to enter a torpid state, but since humans do not hibernate, this reduced metabolism is neither necessary nor healthy. The process may be further exacerbated when these fats become oxidized, as this increases reductive stress.

> *"In the last 100 years, we've eaten more and more and more of these unsaturated fats,"* Marshall says. *"And, of course, the polyunsaturated fats contribute to this process as well because the Delta-6-desaturase is the limiting step in the oxidation of the polyunsaturated fats.*
>
> *You've talked a lot about concerns with polyunsaturated fats, and what I see when I look at it is, linoleic acid (LA) … is okay if it stays as linoleic acid, but once it starts getting converted to oxidized fats, that's when it becomes a real problem."*

Editor's Note 1: *Delta-6-desaturase doesn't oxidize fats itself. As Marshall clarifies in the full interview, it adds a double bond to LA — the rate-limiting step in converting LA to arachidonic acid, which other enzymes can then oxidize.*

Editor's Note 2: *In the full interview, Marshall prefaces this comment by saying LA is "still not my favorite fat." Because LA accumulates in your tissues and readily oxidizes, I recommend keeping your LA intake below 5 grams per day.*

Through a series of enzymatic steps, LA is transformed into arachidonic acid. Arachidonic acid, when oxidized, can form various types of hydroxyeicosatetraenoic acids (HETEs), which are signaling molecules involved in numerous physiological processes, including inflammation and the immune response.

Marshall believes that two HETEs in particular, 5-HETE and 12-HETE, activate two nuclear receptors — the aryl hydrocarbon receptor (AHR) and PPAR-alpha — that he believes help control the shift toward torpor metabolism. In his view, these receptors appear to be controlled in part by the harmful oxidized LA metabolites (OXLAMs) produced when LA is oxidized.

Marshall's proposed path from linoleic acid to a slower, torpor-like metabolism

Proposed mechanism

Linoleic acid (LA)
A polyunsaturated fat

↓

Delta-6-desaturase adds a double bond
The rate-limiting step

↓

Arachidonic acid forms
Other enzymes can then oxidize it

↓

HETEs form when it oxidizes
Including 5-HETE and 12-HETE

↓

Two receptors switch on
The aryl hydrocarbon receptor (AHR) and PPAR-alpha, which Marshall believes help shift metabolism toward torpor

Proposed mechanism described by Brad Marshall.
Source: Mercola J. Interview with Brad Marshall. *Mercola.com*, May 26, 2024.

Figure 2. *Marshall proposes that linoleic acid, once converted to arachidonic acid and oxidized into HETEs, activates two receptors that may shift metabolism toward a torpor-like state.*

The Link Between High-PUF Diets, Metabolic Syndrome, and Related Issues

According to Marshall, oxidizing plenty of PUFs also activates the AHR, which is a nuclear receptor that helps regulate your circadian rhythm. He comments:

> *"If you give a mouse a drug that strongly activates the aryl hydrocarbon receptor, it shuts down the circadian rhythm of the mouse. The aryl hydrocarbon receptor controls your circadian rhythm. And people who have metabolic syndrome have issues with sleep.*
>
> *If you trigger the aryl hydrocarbon receptor, you also get a dysregulated gut microbiome. If you are oxidizing a lot of polyunsaturated fat, you activate the aryl hydrocarbon receptor and all of a sudden you have overgrowth of bad gut bugs and you'll have a decrease in the good gut bugs."*

Marshall notes that it isn't entirely known why AHR activation would shift the gut from beneficial to pathogenic bacteria, but the AHR is highly involved in controlling the immune system. Activating it increases myeloid-derived suppressor cells, which suppress your immune response.

Are Starches Good or Bad? It Depends

At this point in the conversation, Marshall brings up a crucial point. Many in the Ray Peat community believe that starches, especially resistant starches, will promote the growth of pathogenic bacteria that produce endotoxin, also known as lipopolysaccharide or LPS. LPS can get into your bloodstream and cause all kinds of problems, so you don't want a high LPS response.

However, after looking at this issue for the last 18 months, I've started to understand the flaws in Peat's work. One of the primary functions of the gut is to maintain an anaerobic environment (an environment without oxygen). The problem is, you need energy to keep oxygen out of there, and if that energy is not available, oxygen is going to seep in.

Most beneficial gut bacteria are obligate anaerobes, meaning they can't survive in the presence of oxygen. Many of them are gram-positive and have no LPS in their cell wall, and the gram-negative species common in a healthy gut carry a far less inflammatory form of LPS, so they don't trigger the strong endotoxin response that pathogenic bacteria do when they die off. However, when you don't create enough cellular energy you are unable to create a low-oxygen environment in your large intestine.

This kills the beneficial bacteria as oxygen seeps in, and they are unable to survive. When they leave, they create a hole that allows endotoxin-producing bacteria — facultative anaerobes — to take over through competitive inhibition. Facultative anaerobes can tolerate oxygen and survive.

One of the key obligate anaerobic bacteria in your gut is a species called Akkermansia muciniphila, which feeds on mucin — the protective layer lining your gut — and in doing so helps stimulate its ongoing renewal. When your Akkermansia die off due to lack of cellular energy to maintain the proper oxygen gradient in the large intestine, your mucin barrier can start to break down, which can contribute to leaky gut.

Now, the reason starch CAN be problematic is because, if you are metabolically inflexible (and most are), then you're not making enough mitochondrial energy to maintain a healthy gut. So, the idea that starch is problematic may hold true for many people, because so many have a disrupted microbiome. Starch is indiscriminate and will feed any bacteria. So, if your gut is dominated by pathogenic bacteria, starch can cause problems.

The flip side of this is that if you have a healthy gut microbiome, starch can be quite beneficial. So, the primary goal is to get your cellular energy up and improve your microbiome first. Then you can eat starch.

Editor's Note: *Since this interview was first published, I've updated my guidance on restoring gut health. For most adults, I now recommend white rice and whole fruits as the first step for restoring gut function, rather than avoiding starch until your microbiome has improved. Only those with a severely compromised gut need to start more gently.*

Other Feedback Loops That Push Us Toward Metabolic Syndrome

While Marshall agrees with my theory of why starches can cause problems, he points out that there are other feedback loops at work as well:

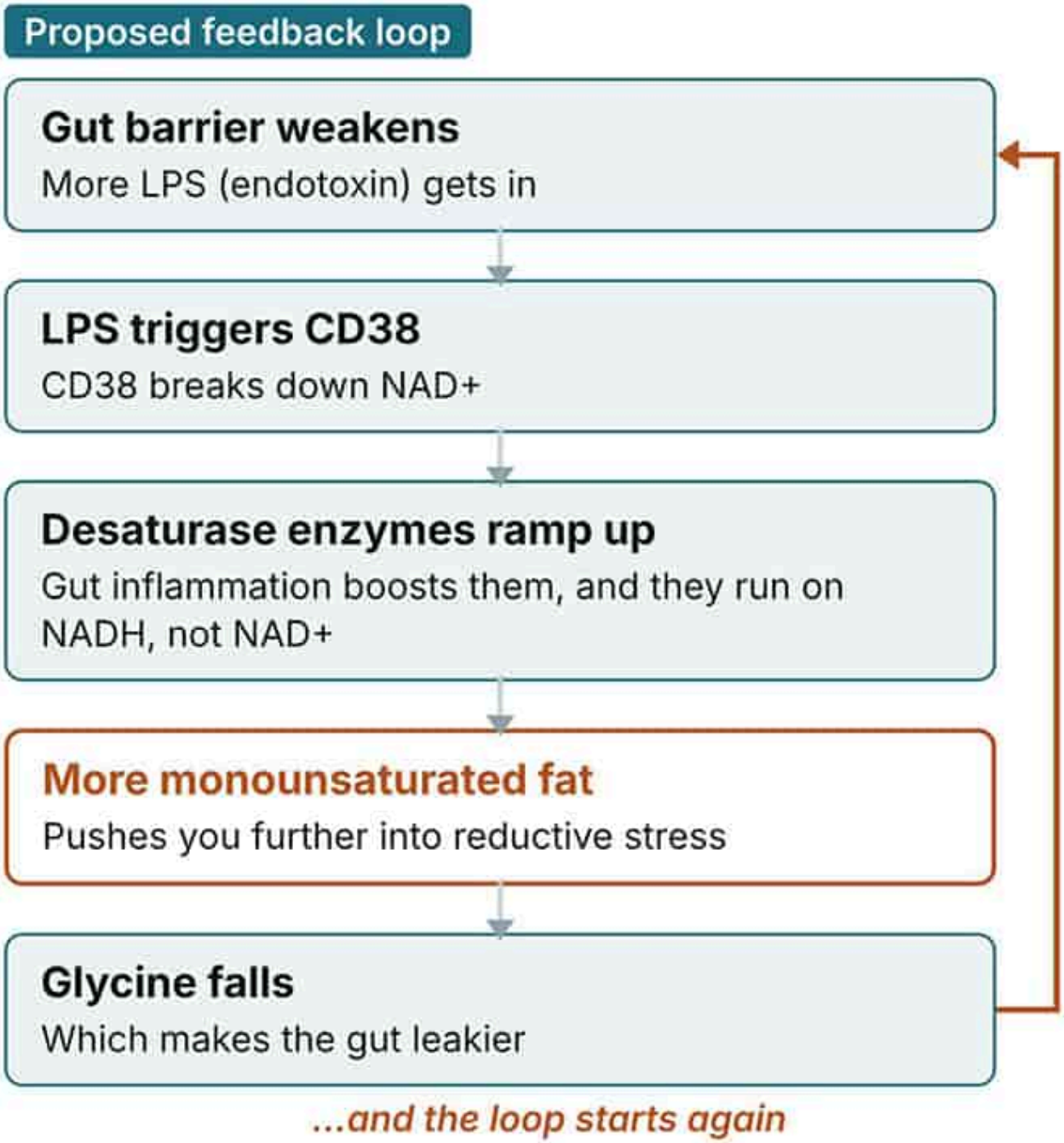
> *"This is all part of one sort of big complicated positive feedback loop. I 100% agree with you about the gut barrier function. But I also think that there's a whole bunch of aligned systems that are pushing us towards this outcome [metabolic syndrome].*
>
> *When you look at the hibernating animals, when they go towards winter and you see all those desaturase enzymes are increased, their gut permeability increases. One of the tricks that the animal does as the hibernating season is approaching is they increase gut permeability, and they let more LPS in.*
>
> *That may also let more oxygen through. I'm not sure. One of the patterns that you see in obesity and metabolic syndrome is that branched-chain amino acids in your bloodstream increase and glycine goes down. In mice, if you supplement with glycine, it increases gut barrier function.*
>
> *So, you have this pattern going into winter where AHR is activated, desaturases are activated, gut barrier function is decreasing and LPS is coming in that causes release of CD38, [which] breaks down NAD+. And so, anytime LPS is coming through, it's decreasing NAD+ availability.*
>
> *The thing about that is, all three desaturases run off NADH and not NAD+. So, the gut inflammation leads to increased activity of these desaturases, which leads to increased monounsaturated fat production, which continues to push*

you further in that direction of reductive stress, which lowers glycine, which makes the gut leakier. To me, it looks like it's all wrapped into the same process.

These processes all work together, and they all work in these feedback loops because if you are an animal in the right situation, you want to have a low metabolic rate, you want to have slow metabolism, and you want to be storing extra fuel.

It's a very complicated process with a lot of different parts, and they're all working together to achieve the outcome, which we call metabolic syndrome. Because in our situation, we don't have to store extra fat for winter and we're not going to hibernate."

Marshall describes a loop that keeps pushing the body toward metabolic syndrome



Proposed loop described by Brad Marshall; the glycine and gut barrier link comes from mice.

Source: Mercola J. Interview with Brad Marshall. *Mercola.com*, May 26, 2024.

Figure 3. *In Marshall's view, a leaky gut, NAD+ loss, desaturase activity, monounsaturated fat, and falling glycine feed one another in a loop that pushes toward metabolic syndrome.*

Tracing the Inflammatory Cascade to Its Root

Marshall also points out research showing mice that lack SCD1, and therefore cannot make MUF, have very low inflammatory markers.

In autumn, hibernating animals increase SCD1, which increases production of MUFs, which, in turn, appears to ramp up inflammatory signaling through TLR4 (a receptor in the gut lining that recognizes bacterial components) and NF-kappa B (a master regulator of inflammation).

At the same time, stearoylethanolamide (SEA) production is reduced. SEA is a bioactive lipid made from stearic acid that has been noted in animal research for its effects on reducing appetite and inflammation. For transparency, Marshall sells an SEA supplement, available through his website.

However, in Ntambi's mouse studies, eliminating Delta-9 desaturase activity largely shut down that whole inflammatory cascade. Marshall suspects that activation of Delta-9 desaturase is one of the primary contributors to the inflammation reflected in elevated C-reactive protein, though he acknowledges that the strongest evidence for this comes from mouse models, which are imperfect. If he's right, reducing Delta-9 desaturase activity may be one way to help calm that inflammatory cascade.

SEA, which is available as a supplement, may help counter the positive feedback loops just described. In rodent studies,[3] SEA has been reported to reduce inflammation, lower production of tumor necrosis factor alpha (TNF-alpha) and suppress SCD1 (Delta-9 desaturase) in the liver. Controlled studies in humans are still lacking.

"So, it's doing all of the things that you would predict would help your metabolic rate," Marshall says. In the interview, he describes the effects his SEA supplement had on his **morning body temperature readings**, which is a simple way to gauge your metabolic

rate, and how he was able to use that to fine-tune his dosage.

What Do Countries with Low Diabetes Rates Eat?

As noted by Marshall, West Africa has some of the world's lowest diabetes rates, and its traditional diet is rich in starchy tubers like plantains, cassava, and African yams, as well as collagenous meats like beef skin. These foods are often used in stews, extracting collagen and gelatin.

This dietary pattern, emphasizing starchy tubers and collagen-rich meats, contrasts with diets higher in processed foods and may contribute to the lower diabetes prevalence seen in some West African countries — below 3%, by Marshall's estimate, compared to around 11% in Spain. Note that this is an observational comparison between populations, so it can't prove that diet is the cause.

My idea of a healthy meal would be white rice cooked in bone broth, topped off with a couple of egg yolks and a small amount of beef liver. This meal would be high in starch and collagen, and low in fructose and muscle meat, which has a very different amino acid composition than collagen. For a refresher on the difference between muscle meat and collagen, see "**Why Collagen Is a Proven Necessity**." Marshall comments:

> *"One of the things about starch is, if you eat a bunch of starch, your NAD+ availability increases postprandially. After the meal, you have more NAD+ availability if you're burning a lot of starch. And so, it all comes down to reductive stress."*

Why Olive Oil Isn't as Healthy as It's Made Out To Be

Marshall also recounts research showing the differences between saturated and unsaturated fats in terms of how they affect your metabolism.

“This experiment has been done in humans about four or five times. They feed people bread and butter or bread and olive oil, and measure how much oxygen they're consuming and how much carbon dioxide they're breathing out. That's called respiratory exchange ratio.

If you look at those two numbers, you can determine how much carbohydrate and fat people are burning. And so, if people eat bread with butter, they'll have a relatively high respiratory exchange ratio, and that means that they're burning a lot of the carbohydrate in the meal. So, you eat bread and butter, you can burn that carbohydrate cleanly, which is the right way to do it.

If you eat bread and butter, you want to burn those carbs first. Then, as your blood glucose levels drop, then you'll start to burn more of the fat from the meal. That's the correct sequence. If you eat olive oil and bread, you burn less of the glucose right away.

I would argue that the olive oil makes you essentially acutely insulin resistant. Because the insulin, you eat that bread, the insulin is signaling, it's trying to clear the other things out to allow that glucose to burn. But if you eat bread and olive oil, your respiratory exchange ratio will be lower, and that means you're burning more fat.

And of course, if you read those articles, they say, ‘Oh, eureka. If you eat olive oil, you'll burn more fat than if you eat butter.’ When I look at that, I say, ‘This is bad. This is not what you want.’”

Olive oil, if pure (and many aren’t, as adulteration with cheaper seed oils is common) is mostly oleic acid, a MUF, but Marshall notes that PUFs have a similar effect — both appear to inhibit glucose metabolism. What’s more, when you consume oleic acid, it creates oleoylethanolamide (OEA), which has the opposite effect of SEA.

OEA activates a nuclear receptor called PPAR-alpha, which, in turn, activates an enzyme called pyruvate dehydrogenase kinase (PDK) that switches off pyruvate dehydrogenase, a key gateway for burning glucose. So, according to Marshall, eating MUF sends a signal

that activates PPAR-alpha, which can suppress your ability to break down glucose from that meal. That's why I recommend using olive oil only in moderation, and favoring saturated fats like tallow, ghee, and grass fed butter for cooking.

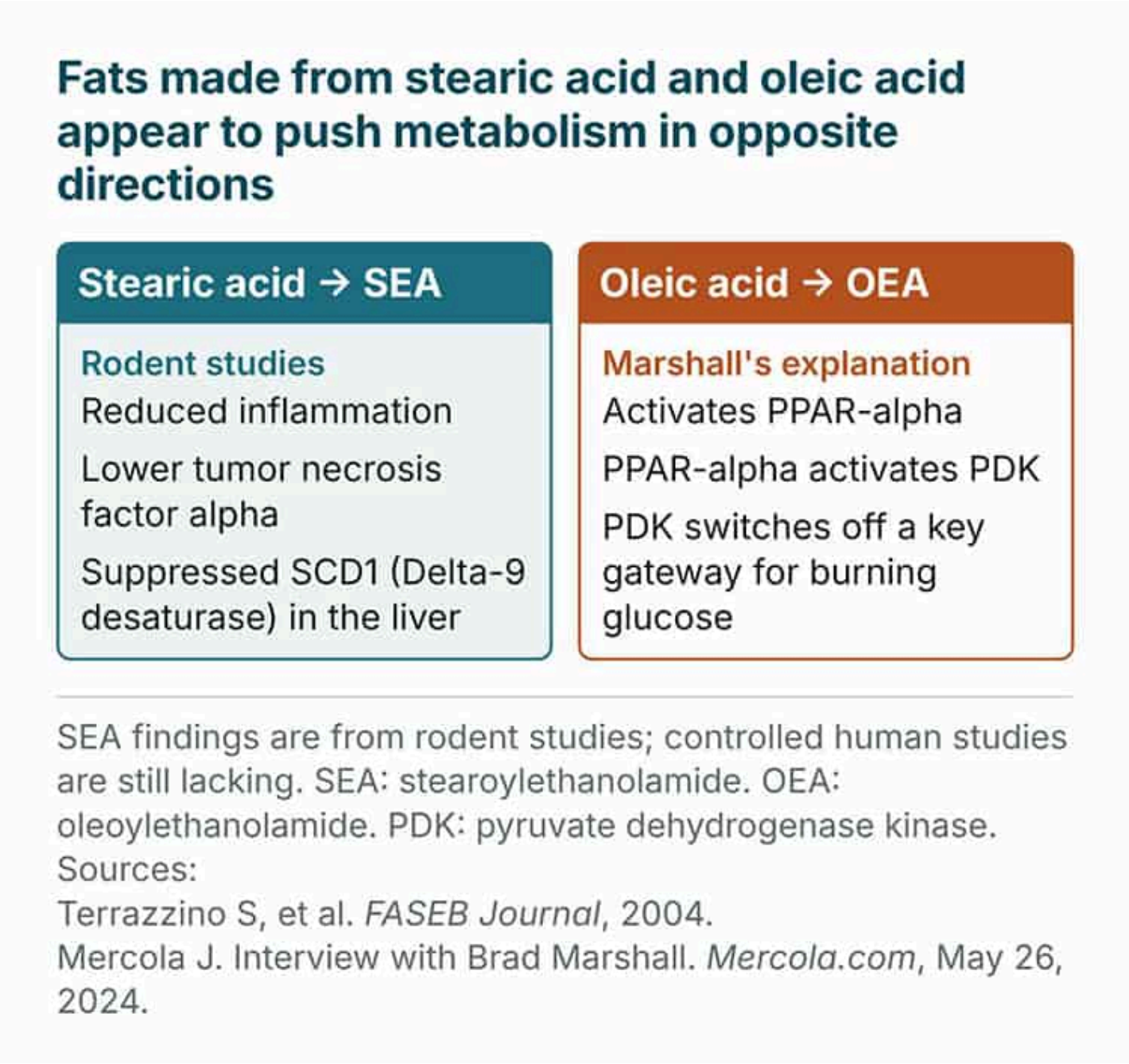


Figure 4. *In rodent studies, SEA from stearic acid reduced inflammation and suppressed liver SCD1, while OEA from oleic acid, according to Marshall, switches off a key gateway for burning glucose.*

High Metabolism Is the Goal

Marshall continues:

> *"If you compare bread and butter to bread and olive oil, the bread and butter looks like that's what you want … as you want to burn those carbs. Because if you burn those carbs, your NAD+ availability will go up. And I said this in the last show, but there's this old saying that 'fat burns in the flame of carbohydrate.'*
>
> *You get that NAD+ availability up and you get that flywheel spinning, and now you can efficiently burn the fat in the meal and also your stored body fat, because the carbs are really driving that process."*

Marshall has been exploring SEA supplementation as one possible way to support this, although its effect on metabolic rate in people has not yet been tested in controlled studies. Remember, the key goal is to increase your body's ability to create cellular energy, which means improving your mitochondrial function and increasing your metabolic rate.

Supporting your cellular energy production gives your body more of what it needs to carry out its own repair and healing processes, which is why I consider it foundational to health.

Again, to summarize, in animal research, SEA appears to counteract the effects of oleic acid by influencing your body's metabolism and its response to fats. It seems to do this, in part, by suppressing the enzyme delta-9 desaturase in the liver, which plays a role in converting saturated fats into MUFs like oleic acid.*

By doing so, Marshall believes SEA may reduce your body's tendency to store fat, mimicking a condition where energy storage for winter is unnecessary. In his view, this may, in turn, support your metabolic rate and help calm inflammation by keeping NF-kappa B, a protein complex involved in inflammatory responses, from switching on inflammatory genes.

**These findings are from laboratory or animal research and may not directly apply to human health.*

More Information

To learn more, please listen to the interview in its entirety. You may need to listen to it several times, even, to really understand it. Once you do, however, the answers to many of your health problems will become that much clearer. And, if you want to dive deeper into molecular biology, be sure to check out Marshall's YouTube channel, **Fire in a Bottle**.

This article is for informational purposes only and does not constitute medical advice. Consult a qualified health care provider before making changes to your health regimen.

Sources and References

- [1] YouTube, Dr. Mercola, Navigating Reductive Stress and the Metabolic Impact of Dietary Fats — Interview with Brad Marshall May 26, 2024
- [2] Proc Natl Acad Sci U S A. 2002;99(17):11482–11486
- [3] FASEB J. 2004;18(13):1580–1582