The Hormone That Links Stress, Mitochondria, Metabolism, and Aging

6 MIN READ

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BY MICHELE ROSS

A metabolic hormone also doubles as a stress response hormone, offering a clue as to how emotional strain becomes physical.

Being stressed **takes energy** â?? literally. Whether youâ??re burning the midnight oil at work, toggling between caregiving roles for your kids and elderly parents, working through a conflict with your spouse, or navigating the daily news, your brain and body have to marshal resources to respond.Â

New research points to a surprising link between how cells make energy and how stress plays out in the body. At the center of it: FGF21 (fibroblast growth factor 21), a metabolic hormone, and mitochondria, the tiny power plants inside our cells. The way these two interact may help explain how psychological stress turns into physical, metabolic change, with possible ripple effects on health and aging.

The Hormone Connecting Stress and Metabolism

Produced primarily by the liver, FGF21 is an important metabolic hormone that helps the body adapt to changing energy demands. Its levels can change in response to fasting, impaired **mitochondrial energy production**, and other forms of

metabolic stress â?? essentially, situations that challenge the bodyâ??s normal energy balance.

Elevated levels are often seen in individuals with **obesity, type 2 diabetes, and metabolic syndrome**, but that doesnâ??t mean the hormone is causing those conditions. It may instead reflect the bodyâ??s attempt to compensate for metabolic stress. (Think of it as firefighters at a burning house: More firefighters doesnâ??t mean they started the blaze.)

While FGF21 has been studied for decades for its role in metabolic health, recent research shows, for the first time, that psychological stress impacts it, too.

An **October, 2025 study** in the journal *Nature Metabolism* tracked responses following acute psychological stress in healthy individuals as well as those with mitochondrial disease. In healthy people, FGF21 levels dropped 20% immediately after being exposed to the stressor, bouncing back to baseline after 90 minutes. In the group with mitochondrial disease, FGF21 levels rose 32%, peaking at 90 minutes. The opposing responses offer an intriguing clue: The way this metabolic hormone responds to psychological stress appears to be shaped, at least in part, by the bodyâ??s capacity to produce cellular energy.

â??This divergence between people with (ab)normal mitochondria tells us that mitochondria somehow mediate the stress-FGF21 response,â?• says **Martin Picard, PhD**, associate professor of behavioral medicine at Columbia, co-director of the Columbia Science of Health program, and senior author of the study. â??Defective mitochondria changes the set of physiological systems recruited by mental stress.â?•

One explanation is that people with the defect experience stress as more severe, Picard says. But he thinks the likelier possibility is that their stress-response systems are working out of sync. When mitochondria canâ??t produce energy properly, the whole mind-body stress response gets reshaped.

In other words: Give two people the same stressful experience, and their bodies may

respond differently depending, in part, on their capacity to produce cellular energy.

Longterm Life Stressors Matter As Much As Acute Stressors

Picardâ??s team also made a fascinating observation when they zoomed out. Drawing on data from more than 20,000 people in the UK Biobank, plus their own ongoing **Mitochondrial Stress and Biomarkers in Emotion (MiSBIE) study**, which explores how energy, mitochondria, and brain-body processes shape health, they looked at FGF21 alongside longer-term stress and well-being.

A pattern emerged. People dealing with loneliness, a history of childhood neglect, or a recent breakup tended to have higher FGF21 levels. Those with more social contact, stronger support, and more satisfying relationships tended to have lower ones.

So FGF21 isnâ??t just reacting to a stressful moment in the lab. It seems to reflect the shape of our social and emotional lives over time.

Again, lower FGF21 isnâ??t necessarily the end goal. According to Picard, thereâ??s no established â??sweet spotâ?• for where you want FGF21 to land. What may matter more is its ability to respond dynamically to changing demands. â??Like most physiological systems, the key is to be able to turn it up and down when needed,â?• he says.

The Metabolic Cost of Psychological Stress

FGF21 doesnâ??t replace what scientists already know about cortisol and the stress response. It adds another potential player: one that directly connects psychological stress with cellular energy metabolism, and a set of related medical conditions.

â??We have fairly strong evidence that chronic or severe stress is associated with poorer metabolic health, including higher risks of obesity, insulin resistance, diabetes, and fatty liver disease,â?• says **Jay Luthar, MD, DipABLM**, founder and medical director at longevity-focused concierge practice Lutanen Health and an instructor at Harvard Medical School.

Say youâ??re faced with immediate threat. Your body canâ??t differentiate a meeting with your boss from a speeding car headed your way. In either case, it mobilizes fuel to give you the resources to respond. Thatâ??s useful when the stress is short-lived. But when that emergency response is on speed dial and gets called on repeat, the same systems designed to protect you can become costly. Everything from glucose regulation and inflammation to appetite and sleep can take a hit, says Dr. Luthar.

Your Mitochondria May Help Determine How Your Body Handles Stress

You probably remember from your high school biology class that mitochondria are the â??powerhousesâ?• of the cell. While true, this description is incomplete. Beyond producing adenosine triphosphate (ATP) â?? the energy currency cells use to do their jobs â?? mitochondria also participate in processes ranging from cellular signaling to inflammation and the stress response.

â??A psychological stressor doesnâ??t require us to run a marathon, but the body still needs to rapidly redistribute energy and resources: heart rate increases, alertness increases, and hormones such as cortisol and adrenaline change,â?• Dr. Luthar explains. In that sense, thereâ??s a clear connection between the brainâ??s stress response and cellular energy metabolism.Â

Still, that doesnâ??t necessarily mean people with â??healthierâ?• mitochondria are more psychologically resilient. But the dramatically different FGF21 response in people with mitochondrial disease suggests that the bodyâ??s capacity to produce

cellular energy influences at least some of the biology underlying the stress response.

The discovery gives researchers a new pathway to investigate as they try to understand how psychological experiences become biologically embedded â?? and whether those changes ultimately contribute to metabolic disease and aging. â??This study shows a mechanism whereby stress gets into our cells to interact with our mitochondria and remodel metabolism,â?• says Picard.

The finding fits into a much broader body of work from Picardâ??s lab examining the relationships among psychological stress, cellular energy, and aging.

In a **recent preprint**, his team reports evidence of chronic stress-system activation in people with mitochondrial diseases. In **previous research**, his team found that mitochondrial energy-production defects were associated with hypermetabolism in people with mitochondrial diseases.Â

In patient-derived cells, those defects were also linked with faster telomere erosion and epigenetic aging â?? providing another clue that disrupted cellular energy metabolism may intersect with aging biology. He says that the **Brain-body Energy Conservation** model suggests how it all fits together. The basic idea: Aging cells can become expensive. As damaged cells demand more energy to maintain themselves, the brain may compensate by conserving resources elsewhere, dialing down lower-priority functions to stay within the bodyâ??s energy budget. This energy trade-off could contribute to some of the changes we associate with aging.Â

Itâ??s a compelling framework, but with an important caveat: Itâ??s a model, not proof that psychological stress directly ages the body through this pathway.

What We Know â?? and What We Donâ??t

Dr. Luthar says these recent findings are compelling but advises against overstating the evidence. â??This was not a study demonstrating that everyday stress causes

mitochondrial disease, that FGF21 causes diabetes, or that changing FGF21 will make people live longer,â?• he says. â??It also doesnâ??t establish that an FGF21 blood test can currently tell us how stressed someone is or how biologically old they are.â?• Instead, the new findings are just one piece of a larger puzzle.

â??We already know that chronic stress can influence metabolic and inflammatory physiology, and that mitochondria are deeply involved in cellular energy management and metabolic disease,â?•Â Dr. Luthar continues. â??The new FGF21 findings provide an interesting potential bridge between the stress response and mitochondrial energy capacity, but more research is required.â?•

Does this altered FGF21 response actually contribute to disease, or is it simply a marker of the bodyâ??s response to stress? Do these findings extend beyond people with mitochondrial disease to the much subtler differences in mitochondrial biology among otherwise healthy people? And can changing FGF21 itself meaningfully change health outcomes?Â

These questions remain unanswered.Â

But, the studyâ??s authors say that understanding the hormonal mechanism could be an important step in addressing metabolic disease.

â??These results reveal a **new axis of vulnerability**,â?• said Mangesh Kurade, lead author on the study at Columbia. â??The way our social environment and psychological experiences interact with mitochondrial health may directly shape metabolic outcomes and long-term disease risk.â?•

The Practical Takeaway

We still donâ??t know for certain if boosting your mitochondrial health will change your FGF21 response to stressÂ â?? or prevent stress-related disease. Still, thereâ??s already **plenty of reason** to support mitochondrial and metabolic health more broadly. The strategies that do so are neither exotic nor costly.

â??For most people, the practical message is reassuring but unglamorous: exercise regularly, sleep adequately, eat a high-quality diet, donâ??t smoke, maintain metabolic health, and develop sustainable ways of managing chronic stress,â?• says Dr. Luthar. No, these habits arenâ??t proven â??FGF21 hacks,â?• and we donâ??t yet know whether theyâ??ll change this particular stress response.Â

Nonetheless, they support metabolic and mitochondrial health â?? both of which you want trending in the right direction for the sake of healthier, more vibrant years.

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WRITTEN BY:

Michele Ross