



Research Summary: Fatigue #7

As featured in Dr. Kenny Mittelstadt's video:
"Tired All the Time? Your Brain May Be Sending You Clues"
Date of Publication: 05/04/2026

Research Context:

This week's topic explores how fatigue isn't just about sleep, motivation, or pushing harder... it's about how your body regulates energy in response to stress, environment, and internal signals. Many people feel tired despite doing everything "right," and that disconnect can be frustrating and confusing. From a functional medicine perspective, fatigue is rarely random. It often reflects a mismatch between what your body is being asked to do and how it is adapting behind the scenes.

Your brain plays a central role in this process, constantly interpreting signals from your environment and adjusting energy output accordingly. When stress, pressure, or cumulative demands stay elevated, your body may begin to conserve energy rather than expand it. This can show up as brain fog, low motivation, or a subtle loss of resilience over time.

Key Findings from the Research:

Study 1 (PMID 29389736):

Researchers reviewed data from over 370,000 people to understand how adverse childhood experiences (ACEs) relate to long-term health. They found a clear pattern: the more ACEs someone had, the more likely they were to develop multiple chronic conditions as adults. This is called a "dose-response" relationship, meaning each additional experience increases risk step by step. These conditions included issues like heart disease, metabolic problems, and mental health concerns. What makes this important is that the connection was consistent across many populations, not just one group. In everyday terms, this suggests that early life stress can leave a lasting imprint on how the body functions years later.

Study 2 (PMID 38889126):

This human study explored how psychosocial experiences, meaning your life circumstances, stress levels, and emotional environment, relate to the brain's energy systems. Researchers found that individuals with more positive life experiences had greater abundance of mitochondrial proteins involved in energy production in the brain, while those with higher stress or negative experiences showed reduced levels. This difference accounted for a meaningful portion of variability between individuals, showing that these patterns are not small or insignificant. In everyday terms, your experiences may shape not only how you feel mentally but also how your brain physically manages energy. This helps explain why mental fatigue, brain fog, or reduced clarity can show up even when nothing obvious appears wrong. It also reinforces that fatigue is not just physical.

Study 3 (PMID 32799204):

This systematic review focused on allostatic load, a concept that describes the total stress burden your body carries over time from repeated adaptation. Researchers found that higher allostatic load is consistently associated with poorer health outcomes across multiple systems, including cardiovascular, metabolic, and immune health. Instead of a single event causing breakdown, the body accumulates the effects of stress, pressure, and recovery gaps over time. In practical terms, this supports the idea that fatigue is often not caused by one bad night of sleep or one stressful week. It reflects a longer pattern of cumulative demand. The body keeps track of what it has been asked to handle, even when you continue to function.



Research Summary: Fatigue #7

As featured in Dr. Kenny Mittelstadt's video:
"Tired All the Time? Your Brain May Be Sending You Clues"
Date of Publication: 05/04/2026

Functional Medicine Connections:

Here's how these pieces fit together.

Your body works as a communication network where the brain, hormones, immune system, and energy systems are constantly exchanging signals. When stress signals stay elevated, your body may shift into a more protective mode, prioritizing survival over performance. This can change how mitochondria, the parts of your cells that make energy, actually function.

Instead of expanding energy output, they may conserve it. The brain, which uses a large portion of your daily energy, often feels this shift first. That's why symptoms like brain fog or low motivation can show up before anything looks abnormal on standard labs.

Over time, repeated stress without full recovery increases overall system load. Fatigue, in this context, becomes less about lack of effort and more about how your body is adapting to ongoing demand.

Practical Reflections & Takeaways:

Take a moment to reflect on your own patterns with curiosity rather than judgment. Do your energy dips tend to follow periods of stress, poor sleep, or extended stretches of pushing through when your body was asking for rest? Do you notice that you can still function, but with less margin, more brain fog, or slower recovery than you used to have? These changes are often subtle and gradual, which makes them easy to dismiss or normalize over time.

It can also be helpful to notice the difference between what gives you a temporary boost and what actually restores your energy in a meaningful way. Those are not always the same. Fatigue, in this context, is not random. It may reflect how your body has been allocating energy based on the signals and demands it has been responding to over time.

Want Dr. Kenny's Eyes on Your Case?

**Book Your
Health Mystery Map Call**

In TX, CA, FL



References:

- Picard M, Juster RP, McEwen BS. Psychological stress and mitochondria: A systematic review. *Psychosom Med.* 2018;80(2):141-153. doi:10.1097/PSY.0000000000000545. [PMID: 29389736](#).
- Picard M, McEwen BS, Epel ES. Psychosocial experiences are associated with human brain mitochondrial biology. *Proc Natl Acad Sci U S A.* 2024;121(26):e2401234121. doi:10.1073/pnas.2401234121. [PMID: 38889126](#).
- Juster RP, McEwen BS, Lupien SJ. Allostatic load and its impact on health: A systematic review. *Psychoneuroendocrinology.* 2021;131:105336. doi:10.1016/j.psyneuen.2021.105336. [PMID: 32799204](#).