Research Summary: Fatigue #6

As featured in Dr. Kenny Mittelstadt's video:
"Why Am I Always So TIRED? 15 Root Causes of Low Energy and Constant Fatigue"
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Research Context:

This week's topic explores why feeling tired all the time isn't just about sleep, motivation, or doing something wrong. For many people, fatigue shows up even when labs look "normal," which can feel confusing and frustrating. From a functional medicine perspective, this often means the issue hasn't been fully interpreted yet, not that nothing is happening.

Instead of pointing to one clear cause, fatigue usually reflects how multiple systems in your body are managing energy at the same time. Your stress response, blood sugar regulation, mitochondrial energy production, immune activity, and nutrient status are all constantly communicating. When enough of these systems are under strain, your body may begin to conserve energy rather than spend it.
The research below helps connect these dots.

Key Findings from the Research:

Study 1 (PMID 32886587):
This large review looked at how chronic stress affects the body and found that it doesn't stay isolated to one system. Instead, it creates what researchers call "allostatic load," which is the cumulative wear and tear from ongoing stress exposure. Over time, this affects your brain, hormones, immune system, and metabolism all at once. One of the most important findings is that chronic stress can shift how your body regulates energy. Instead of prioritizing performance, focus, or recovery, the body begins to conserve energy as a protective response. This can show up as fatigue, poor sleep patterns, brain fog, or reduced resilience to everyday stressors.

Study 2 (PMID 36091835):
This systematic review and meta-analysis examined multiple randomized controlled trials using CoQ10, a nutrient that plays a key role in mitochondrial energy production. Mitochondria are the structures in your cells responsible for generating usable energy, and CoQ10 is part of the process that allows this energy to be created efficiently. Across the studies reviewed, researchers found that individuals supplementing with CoQ10 experienced measurable reductions in fatigue compared to control groups. While this doesn't mean CoQ10 is the solution for everyone, it provides strong human evidence that improving mitochondrial function can directly impact how energy is experienced. What this means for you: Fatigue is not just about how much sleep you get or how hard you're working. It can reflect how well your cells are producing energy. If that process is impaired, even small inefficiencies can add up over time and show up as persistent low energy.

Study 3 (PMID 36870101:
This systematic review and meta-analysis looked at how caffeine affects sleep quality, even when consumed earlier in the day. Researchers found that caffeine can reduce total sleep time, delay the onset of sleep, and decrease the depth of sleep cycles that are critical for recovery. What's important here is that these effects can happen even when people feel like they are sleeping "enough." In other words, sleep quantity may look fine, but sleep quality is being quietly disrupted. This creates a pattern where people rely on caffeine to push through fatigue, but the caffeine itself contributes to poorer recovery, which then reinforces the fatigue cycle.

Functional Medicine Connections:

Here's how these pieces fit together. Your body doesn't run on one system at a time, it runs on communication between systems that are constantly adjusting to your environment, stress levels, and daily demands.

Your mitochondria, which produce energy, rely on stable input from your hormones, nervous system, and nutrient status. When stress stays high, your brain signals your body to conserve energy instead of spending it freely. This is part of your stress response, often referred to as the neuroendocrine system, which includes your brain and hormone signaling working together.

At the same time, blood sugar swings, inflammation, poor sleep, or even subtle nutrient gaps can create additional "withdrawals" from your energetic reserves.

This is why fatigue rarely comes down to one cause. It reflects overall system load. When enough inputs stack up, your body shifts into a more protective, energy-conserving mode rather than maintaining high output.

Practical Reflections & Takeaways:

Think about your own patterns for a moment. When you look back at your lowest energy days, do they tend to follow certain rhythms like poor sleep, higher stress, or inconsistent meals? Or do they seem to show up without a clear explanation on the surface?

You might also notice that your fatigue feels different depending on the situation. Some days it's physical, other days it's more mental or emotional. These differences can be clues about which systems are under the most strain.

Zooming out can be helpful here. Does your energy change based on your environment, your workload, or how well you've been able to recover?

These patterns are not random. They are signals. When you start to notice them, you're beginning to see how your body is communicating where support may be needed most.

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