The Physical Basis of CFS

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(Editor's note: This is an excellent summary article with detailed references that you can take to your health care providers.)

Often, when people hear that there is no known test or cause for chronic fatigue syndrome (CFS), they mistakenly understand that to mean that the illness is not real. This is incorrect. Over the past 15 years, scientists have identified numerous biological abnormalities that provide evidence for the reality and seriousness of CFS, even though the cause of CFS and diagnostic tests for it are still unknown [1]. These biological abnormalities have given researchers clues to the cause of the illness. In particular, they have provided evidence that the illness involves both the brain and the immune system.

There are no diagnostic tests yet for CFS because none of the biological abnormalities clearly distinguishes patients with CFS from other individuals. In reality, there are no perfect biological tests for any illness. When a test gets close enough to perfect, clinicians use it to help confirm or refute their clinical judgment. Testing in CFS has primarily been used to rule out other illnesses that also can cause chronic fatigue.

What Is The Cause Of CFS?

The leading model of CFS pathogenesis is rooted in scientifically identified abnormalities in the brain (central nervous system) and the immune system, which influence and alter the function of the other in a reciprocal cycle.

Low levels of circulating cortisol, identified in several CFS research studies [2,3] can increase immune activation, which is also a key feature of CFS.

This immune system activation could theoretically result in brain dysfunction: when the immune system is activated, it makes chemical messages. Brain cells as well as other immune system cells can receive these messages. This could lead to fatigue, cognitive dysfunction, enhanced sense of pain, hormonal dysregulation and other features of CFS [4].

Post-Viral Onset

Many cases of CFS begin with symptoms suggesting an infection, like a common viral illness. Doctors do not usually perform tests to confirm common viral infections, since they typically quickly resolve. For that reason, there is no documentation of the infection that seems to start CFS in many patients.

However, some of the most interesting research in recent years involves studies that did document an infection at the start of the illness. For example, CFS has been reported following acute mononucleosis [5,6] (a viral infection), Lyme disease [7-9] (a bacterial infection) and Q fever [10] (an infection with a different kind of infectious agent). These studies prove that CFS can indeed follow in the wake of a well-documented infection.

This research indicates that no single infectious agent is likely to be the cause of CFS. Instead, CFS is likely to be caused by some abnormality in the body's response to any of several different infectious agents. The studies of infectious agents in CFS are complicated. One reason is that the symptoms of CFS almost surely arise from the brain, yet it is very hard for scientists to study infectious agents in the human brain: that requires taking brain tissue (biopsies), a potentially dangerous test.

Another reason is that some infectious agents permanently live in a dormant state inside our bodies. There is evidence that some of these infections, like infection with the virus HHV-6 [11-14], get reawakened in patients with CFS. The unanswered question is whether the reawakened virus is the cause of the bodily damage, and resulting symptoms, or whether it is result of the illness.

Immune System Abnormalities

Several immune system patterns are seen more often in patients with CFS. The identified abnormalities mimic the immune pattern of a body fighting a virus, even though no virus has been identified as the cause of CFS. Specific findings include:

- Increased numbers of CD8+ activated "cytotoxic" T-cells (cells commonly increased when the body is fighting viral infections) [11,15-17]
- Low natural killer cell function [18-21]
- Elevated immune complexes [22]

The most intriguing recent immunological finding in CFS is the discovery of a novel, low molecular weight protein in an antiviral path way called the RNase-L pathway [24-27]. This novel protein is found much more often in CFS patients than in healthy people, or people with two other conditions that can cause fatigue: depression or fibromyalgia [27].

Neurological Findings

There is considerable evidence that the brain and central nervous system are involved in CFS. "Soft" evidence includes patient-reported symptoms such as: cognitive dysfunction; sensitivities to stimuli such as bright lights, noise and odors; numbness and tingling in the extremities; and disordered and fragmented sleep. "Hard" evidence includes:

- Hyperintense signals on MRI scans [11,28,29]
- Reduction in cerebral blood flow on SPECT scans—an abnormality that changes over time, and is not an indication of any permanent brain damage [30,31]
- Autonomic dysfunction, primarily orthostatic intolerance and neurally-mediated hypotension seen on tilt table tests [32-37]. The control centers for maintenance of blood pressure lie in the brain's limbic system.

Epidemiology

Recent epidemiological data has helped to establish the relevance and importance of CFS as a serious public health issue. Data from private investigators and from the Centers for Disease Control and Prevention (CDC) indicate that more than 200 of every 100,000 Americans have CFS [38-40]. Depending on demographic factors—such as age, sex and ethnicity—the prevalence can range from 200 to 800 cases per 100,000 [38]. This makes CFS more common than well-known illnesses such as multiple sclerosis [41] and systemic lupus erythematosus [42], which, like CFS, predominantly affect females.

CFS Is Real

Taken together, these and other findings provide important evidence that CFS is not "all in the head" or an imagined illness. While there is not yet a test, scientists are moving closer to developing tools to assist clinicians in the diagnosis of CFS. In the interim, scientists have provided clues to the biology of CFS and have given clinicians, scientists and patients critical data that shows that CFS is a real and serious illness.

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