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Have we been looking at Multiple Sclerosis all wrong?

Multiple sclerosis is a confusing disease. Widely regarded as an autoimmune problem, it affects millions of sufferers, and we still don't have a complete grasp of what causes it. Part of this problem is due to the fact that every time we find something that seems to be a factor in how it works, that factor doesn't seem universal. But now there's a new theory of MS that could lead to a radically different treatment for the disease.

A new meta-analysis by Dr. Angélique Corthals proposes that much of the difficulty we have with understanding the causes of MS may be because we're wrong about its basic mechanism. In a publication in *The Quarterly Review of Biology*, she proposes that rather than an autoimmune disease like previously supposed, MS might in fact be a metabolic one with an immune component.

It's a bold assertion to be sure, and one without original data to back it up (at this point, anyway). With MS, the myelin which protects and insulated the nerve tissue on your brain and spinal cord swells, and then scars, leading to neuronal damage. Corthals' theory gives another framework to approach this damage, and one with links to a disease we do understand — atherosclerosis. This is where things get a bit dense, so bear with me.

There are certain environmental and genetic factors which can impair PPARs (peroxisome proliferator-activated receptors), which is part of the system that controls the metabolism of fat as well as immune response. When it's running at partial power, the PPARs can't properly control the levels of LDL — the infamous bad cholesterol — which leads to a build up of an oxidized toxic derivative of LDL called oxLDL in the blood. Once these are in the system, Corthals believes the body is "primed" for MS, and it can be triggered by a number of causes, including Epstein-Barr Virus, which is linked to MS in its own right.

Once triggered, an immune system chain reaction starts. The body sends out macrophages to deal with a pathogen, but the macrophages incorrectly gorge themselves on oxLDL. This puts them in a "zombie state", where they don't die and can't empty their contents, instead just building up plaques which damage the myelin sheath, and cause the symptoms of MS.

Edited to clarify: At this point, the disease triggers the immune problems we know of as MS. The theory isn't discarding the immunological side of the disease, just citing metabolism as a root trigger, which leads to the problems of the immune response.

Said Corthals: Eventually, the toxic macrophages are cleared, leading to the remission part of the RRMS (relapsing-remitting MS) cycle. But this detente holds only until the next trigger comes along.

Dysfunction of the PPAR is further implicated in MS because it slows the repair mechanism of the central nervous system to a crawl, preventing the efficient renewal and synthesis of myelin.

It's a novel theory, and while Corthals is working on pulling together some empirical data to back it up, it does answer some of the issues with how MS manifests. The disease has been linked previously to low levels of vitamin D, and is on the uptick in recent decades. Low vitamin D and a diet high in both saturated fat and carbohydrates (which is likewise on the rise) both contribute to the impairment of PPARs.

The mechanism that Corthals suggests is also interesting because it's incredibly similar to that of atherosclerosis. Atherosclerosis is when PPAR failure causes plaque buildup and scarring in arteries, which is the equivalent to what's being described happening to myelin. Also interestingly, men are far more likely to have atherosclerosis and women to have MS, which Corthals suggests may be because of the different way sexes metabolize fats. In the paper, she recommends "multiple sclerosis should be thought of as a metabolic disease, the female equivalent of atherosclerosis, not as a disease of the immune system."

If the raw data bears out this theory, it would mean a radically different approach to the treatment of a major chronic disease. One based on lipid metabolism (and potentially diet) rather than targeting the immune system directly. If it holds up, it would be a major paradigm shift in the way MS is handled — but first we need to see if the data fits the theory.