MICROBIOME LABS

Alzheimer's Disease:
The Gut-Brain Axis

Alzheimer's disease (AD) is a progressive form of dementia that destroys memories and other cognitive functions in the brain. This chronic neurodegenerative disease is the 6th leading cause of death in the US, affecting over 5 million Americans. Scientists believe that damage to the brain likely begins a decade or more before memory loss and other cognitive symptoms arise. During this preclinical stage of AD, protein pieces called beta-amlyoid can clump together between nerve cells forming hard, insoluble plaques and tangled fibers throughout the brain. These plaques and tangles essentially slow down or clog the signals being sent through the nerves to the brain. Some neurons can even be cut off by these amyloid plaques, causing nerves to lose function and die.

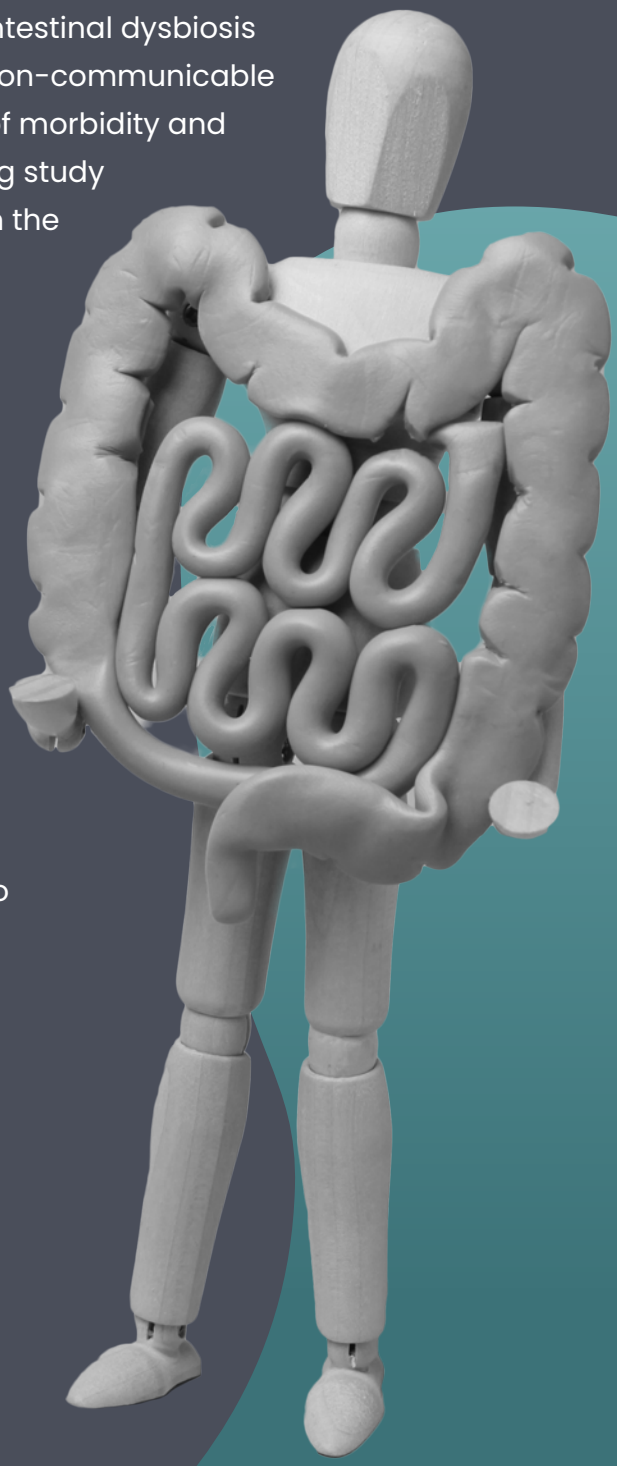
The initial damage appears to take place in the hippocampus, where memories are formed. However, as more nerve cells die, the damage continues to spread to other parts of the brain, and the brain tissue begins to shrink. While the underlying cause of AD is not fully understood, more and more research continues to highlight the important bi-directional connection between the gut microbiome and the brain.

One such study, published September 2017 in the *Frontiers in Immunology* journal, found that patients with AD had high levels of a specific toxin that had accumulated in certain areas of the brain, including the neocortex (responsible for sensory perception, cognitive function, motor function, spatial reasoning, and language) and hippocampus (responsible for motivation, emotion, learning, and memory). This particular toxin is a well-known inflammatory toxin that originates from the gut microbiome known as lipopolysaccharide (LPS).

Lipopolysaccharide, or LPS, can be found in the membrane of Gram-negative bacteria, which make up the majority of the gut microbiome. However, these Gram-negative bacteria play an important role in the gut microbiome.

When these Gram-negative bacteria die, they release LPS from their cell membranes, and it begins to float freely throughout the intestines as a bacterial endotoxin (toxin produced inside the body). Floating around in the intestines, LPS is mostly harmless. However, if there is damage to the intestinal lining, then LPS can enter into the bloodstream, where it can trigger an innate immune response, resulting in sub-clinical, persistent, and low-grade inflammation anywhere in the body. This condition is better known as metabolic endotoxemia.

Metabolic endotoxemia is a condition that stems from intestinal dysbiosis and a breakdown of intestinal barrier function. Among non-communicable diseases, metabolic endotoxemia is the leading cause of morbidity and mortality worldwide. The findings of this ground-breaking study show that LPS accumulates and creates inflammation in the AD brain, highlighting metabolic endotoxemia as an important contributor in inflammatory neurodegenerative diseases like AD.



Interestingly, meals that are high in saturated fats and dense in calories seem to impact the condition more so than low-fat, low-calorie meals. This increase in serum endotoxin concentration is followed by systemic inflammation that is marked by measurable increases in interleukin-6, interleukin-1-alpha, interferon-gamma, triglycerides, and post-prandial insulin. Chronic metabolic endotoxemia and the associated inflammation have been shown to have significant correlation to a variety of chronic diseases. To date, studies support a strong correlation between metabolic endotoxemia (ME) and the risk or onset of conditions such as cardiovascular disease, diabetes, obesity, hypogonadism, autoimmunity, and even mood disorders such as anxiety and depression.

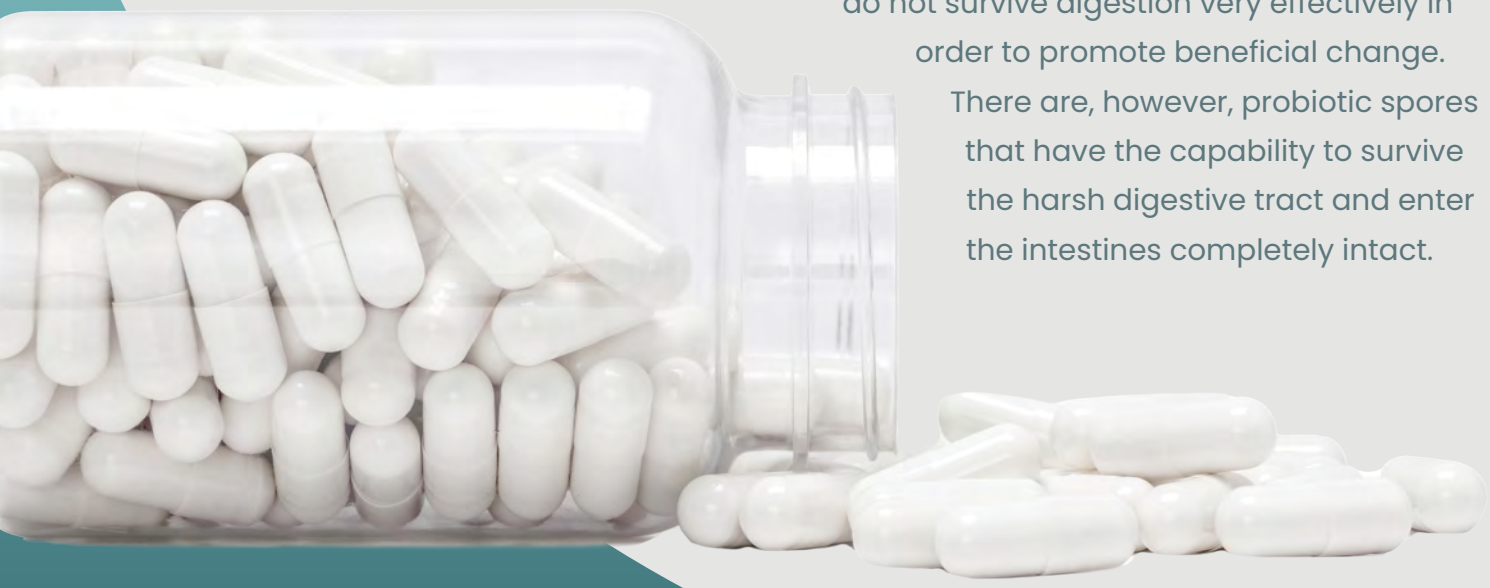
Fortunately, there are some basic lifestyle choices that can help reduce the risk and incidence of ME. Minimizing alcohol consumption, giving up smoking, consuming a variety of different foods, and reducing saturated fat intake can all have a drastic and rapid impact on gut

inflammation and therefore brain health. In addition to the above lifestyle modifications, there are some promising interventional targets that could help decrease endotoxemia including: boosting secretory IgA levels, increasing mucin production, and modulating the microbiome.

Secretory immunoglobulin A (sIgA) is the first line of defense against free-floating LPS in the intestines. This free LPS can eventually make its way through the intestinal lining and into circulation, thereby causing ME. sIgA has the capability to bind and neutralize LPS in the intestines. Thus, increasing sIgA production could have a meaningful impact on reducing inflammation in the gut and brain. Nutrients that have been shown to have a positive impact on the production and secretion of IgA are essential omega-3 fatty acids, glutathione, glycine, glutamine, phosphatidylcholine, vitamin C, zinc, and colostrum.

Another promising intervention is to increase intestinal mucin production. The intestinal mucosa is a key barrier that protects the intestinal lining from toxins like LPS. When the intestinal mucosa is damaged, it fails to perform its barrier function and allows LPS to enter circulation, where it can accumulate anywhere in the body to promote inflammation. Increasing mucin production can help to protect the intestinal lining from LPS so that it leaves the body through excretion. Nutrients that have been shown to support increased mucin production are L-threonine, L-serine, L-proline, and L-cysteine.

Finally, spore-based probiotics hold great promise in modulating the microbiome and supporting a healthy inflammatory response in the body. It is clear that dysbiosis drives inflammation; and as a result, a healthy microbiome has the capability to protect the body from endotoxemia. The major issue with most probiotics is that they do not survive digestion very effectively in order to promote beneficial change. There are, however, probiotic spores that have the capability to survive the harsh digestive tract and enter the intestines completely intact.



To date, bacterial spores are the only probiotics that have been shown to reduce metabolic endotoxemia. Probiotic spores in the product MegaSporeBiotic™ were the subject of a university, double-blind, and placebo-controlled trial to evaluate the ability of the product to reduce or prevent metabolic endotoxemia induced by a dietary challenge meal. In addition to assessing changes in dietary endotoxemia, the researchers also measured how this probiotic altered changes in cardiovascular disease (CVD) risk factors, other novel disease risk biomarkers, and the immune system itself, following a high-fat challenge meal.

Healthy volunteers were screened for the metabolic endotoxemia response to the challenge meal. If they showed the response, they were enrolled into the study and randomized into either the placebo group or treatment group. They consumed the placebo or treatment product for 30 days, with no other interventions or dietary/lifestyle changes. After the 30 days, they reported back to the lab for their "post-treatment" response and were given the same challenge meal. All the same blood work was run to assess their levels of endotoxemia.

The data showed a clear shift to a protective microbiome within just 30 days of supplementation of the spores. The post-test challenge in the treatment group showed a 45% reduction in endotoxemia, whereas in the placebo group had progressively worsened. When compared to the placebo group, the treatment group demonstrated a 60% reduction in LPS levels after only 30 days of supplementation with probiotic spores.

These findings suggest that the probiotic spores were able to strengthen the integrity of the intestinal lining to keep endotoxins like LPS out of the bloodstream. Furthermore, this study suggests that probiotic spores may be one of the most promising therapies available for metabolic endotoxemia and its associated neurological conditions.

References

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