Gut microbes are the initiators of neurodegenerative diseases [1-3] is getting to become recognized [4]. In our research, we hope to find an antibacterial activity (preferred Gram Selective) and destruction of Aβ Fibrils [5].

A connection between Parkinson’s and Irritable bowel syndrome (IBS) caused by a combination of Veillonella and Lactobacillus human microbiome dwellers was investigated. It is acknowledged that for functional gastrointestinal disorder diagnosis, the presence of obvious anatomical or physiological abnormalities should be excluded and that autonomic dysfunction and other neurodegeneration associated with Parkinson’s disease (PD) could be characterized as such abnormalities. More recently there has been recognition of an inflammatory component to the pathology of neurodegeneration, most notably in Alzheimer’s disease (AD) but also in Parkinson’s disease (PD) and motor neuron disease (MND). The last few decades have afforded opportunities to investigate how inflammation and neurodegeneration in the CNS are related to each other, although we are still some way from achieving a full understanding of the complex interactions that can take place [6].

Recently, many publications [7] deal with the potential contribution of pathogenic microbes to aging and AD. Gut bacteria and other microbes and proteins are penetrating the damaged Blood-Brain Barrier (BBB). Once inside the CNS, C. pneumonia, for instance, can infect microglia, astrocytes, and neurons. They are attacking the neurons causing inflammation in the brain. This inflammation is the initial step towards the developments of fatal diseases: Alzheimer’s, Parkinson’s and more of the dozens known illnesses of the brain.

Citation: Dr. Shimon E Shatzmiller. “Gut Microbes Start Neurodegeneration - The Inflammation Approach”. EC Pharmacology and Toxicology SI.01 (2017): 01–03.
The natural immune systems apply antimicrobial peptides, $\beta$-defensin for example and other such agents like Amylin, Amyloid – $\beta$ (A $\beta$ ) are called to defend the neurons, to stop the inflammation. These antimicrobial agents bring with them a “bad” feature: they form aggregates, fibrils, tangles and other supramolecular structures. Theses in the inflamed brain created bodies damage the most sensitive regions of brain neurons, the synapses. The bring atrophy and death by damaging the synapses membrane in an antimicrobial way; digging holes in the cell membranes.

It is More than constipation - bowel symptoms in Parkinson’s disease and their connection to gut microbiota [8]. If the connection between PD, IBS and microbiota are confirmed by further studies, PD research and management could profit from the accumulating evidence on the pathophysiology and treatment of IBS [9].

A model based on initiation of the neurological disorder starts in the invasion of gut fauna to the brain where an inflammation starts [10]. Antimicrobial peptides production as the basis is in the immune system [11] in many ways: diabetes insulin, Amylin, APP and natural $\beta$ -defensins [12] and other in the organism active AMPs. However, these AMPs are forming aggregate and fibrils that destroy the synapses of the neurons in an antimicrobial manner, leading the death (eradication) of the neurons (see cartoon above).

The drug candidate Semagacestat [13] is an azepine containing peptide mimic from natural sources; it reached phase III in the FDA approval ladder. Azepine containing materials were retested as secretase inhibitors. Mant azepine derivatives were tested but as the leading SEMAGACESTAT failed phase III tests, this approach was slowed down.

Generally, there is a feeling that the leading A $\beta$ hypothesis did not deliver remedy to the sick. Novel pursuit of some that were in the near past were expressed ideas, that include A $\beta$ are penetrating the neurodegeneration area, one of them is “inflammation” and combat against this including the supposed earliest stage of the diseases.

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Bibliography


