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Gut microbiome marks Alzheimer's disease

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We reported the induction of neurotoxicity and neurodegeneration by tryptophan metabolites that link the metabolic alterations to Alzheimer's disease (AD). Tryptophan is a product of Shikimate pathway (SP). Human cells lack SP, which is found in human gut bacteria using exclusively SP to produce aromatic amino acids (AAA). The presented study is a first attempt toward gene targeted analysis of human gut microbiota in AD fecal samples. The oligonucleotide primers newly designed for this work target of SP-AAA in environmental bacteria that is associated with the human activity. Using polymerase chain reaction (PCR) we found unique gut bacterial sequence in most AD patients (18 of 20) albeit rarely in controls (1 of 13). Cloning and sequencing AD-associated PCR products (ADPP) enable the identification of Na (+)-transporting NADHu. Biquinone reductase (NQR) in Clostridium sp. The ADPP of unrelated Alzheimer's disease (AD) patients possess near identical sequences. NQR substrate ubiquinone is a SP product and also a human neuroprotectant. A deficit in ubiquinone has been determined in a number of neuromuscular and also in neurodegenerative disorders. The antibacterial therapy has prompted the ADPP reduction in ADPP-positive control person who has been later diagnosed with Alzheimer's disease (AD)-dementia. We explored the gut microbiome databases and uncovered a sequence similarity up to 97% between ADPP and some healthy individuals from different geographical locations. The difference in gut microbial genotypes between Alzheimer's disease (AD) and controls revealed in this study is the breakthrough finding. The test is suggested for a non-invasive laboratory monitoring of Alzheimer's disease (AD) and related/associated disorders.

Introduction:

The recent technological advances have increased the interest on the relationship between the microorganisms inhabiting the gut microbiota and also the human health. The gastrointestinal tract hosts over 100 trillion microorganisms including at least 1000 different species of bacteria. In humans about 1/3 of gut microbiota is common. While the other 2/3 is different from one individual to the another providing our personal identity. Despite the difficulties in defining a good microbiota, data suggest that in the adulthood. A healthy microbiota is characterized by the community stability and the species diversity. More specifically despite lifestyle and food changes the Firmicutes (such as Lactobacillus) and the Bacteroides represent the main bacterial phyla in the gut followed by Proteobacteria, Actinobacteria such as Bifidobacterium, and Cyanobacteria. Which constitute an ecological community entertaining a beneficial relationship with the host. As a result an imbalance of the intestinal bacteria representation could lead to the different diseases that are ranging from inflammatory bowel disease to the obesity, diabetes, and asthma, as well as Parkinson's disease, Alzheimer's disease (AD), and depression.

The Gut-Brain Axis:

In particular millions of nerves end in the gastrointestinal tract mucosa constituting the enteric nervous system which regulates the intestinal functions and communicates with the brain through the vagus nerve. The latter is responsible for the transmission of signals from the brain to the gastrointestinal tract (through the autonomic nervous system) and vice versa. The presence of dysbiosis causing the breakdown of the intestinal permeability can lead to an inflammatory condition not limited to the gut. Since the proinflammatory cytokines can get into the bloodstream and reach to the brain. The importance of the inflammation should not be underestimated since several evidences support its crucial role in several chronic disorders such as type 2 diabetes, Alzheimer's disease (AD) and depression.

Apart from the cytokines and other mediators can send signals from the gut to the brain through the vagus nerve. In fact, especially after a meal rich of fats and carbohydrates, a subgroup of specialized intestinal cells, named as enteroendocrine cells that releases hormones and peptides such as 5-hydroxitryptamine (5-HT), cholecystokinin (CKK), glucagon-like peptide-1 (GLP-1), and peptide YY (PYY). These mediators exert many important functions. For example PYY and GLP-1 inhibit the intestinal peristalsis and improve the glucose metabolism attenuating pancreatic islet hypertrophy and the insulin resistance. Moreover these peptides binding to their cognate receptors located in the nucleus of the solitary tract and in the hypothalamus induce the sense of satiety and modulate the energy expenditure. In addition to this the GLP-1 seems to be able to upgrade hippocampal neural plasticity improving cognition and to stimulate the receptors located in the amygdala and in the hippocampus. Thus exerting anxiolytic and antidepressant effects.

The gut microbiota and brain are strictly intertwined and communicate through different ways including the production of bacteria metabolites, cytokines, and neurotransmitters. On this ground it is not surprising that it has been hypothesized that the gut microbiota could play a pivotal role in the pathogenesis of chronic disorders such as depression, Alzheimer's disease (AD), and diabetes.

Conclusion:

Dysbiosis has been demonstrated to exert the regulatory functions on inflammation and OS and that represents a pathogenetic contributor shared by Alzheimer's disease (AD),

depression, and T2DM these three disorders characterized by a prooxidative and proinflammatory condition. The gut-brain axis can account for the molecular similarities linking to these disorders and also confirmed by the high rates of comorbidity between depression and T2DM which in turn increase the risk of dementia. Metabolism, cognition, and mood are strictly intertwined if glucose toxicity can directly interfere with the cognitive functions. The insulin pathway is involved in amyloid formation, while depression can precipitate neuronal damage through the inflammatory mechanism. Depending the knowledge on the pathogenetic mechanisms of these burdening disorders could open new scenarios. In fact that the manipulation of the gut environment could be further investigated as a preventive and or therapeutic tool with potentially a good safety profile.