Title: Pilot feasibility study probing the role of the microbiome as a mechanism of mediating signaling along the gut-brain axis in major depressive disorder.

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Overview/Abstract

Neuroinflammation (NI) is implicated in the pathophysiology of major depressive disorder (MDD). There have been reports in the literature that bacteria and other microbes, or “microbiota,” of MDD is altered compared to healthy individuals. We are interested in probing the role of the microbiome in mediating signaling along the gut brain axis in MDD. Ultimately, the approach to testing the causal role of the microbiome in increased neuroinflammation in MDD is by treating these patients with probiotics to “normalize” their microbiome. However, reports differ as to which bacterial taxa exhibit different relative abundances in MDD vs healthy individuals without psychiatric disease. Therefore, it is important to first identify which bacteria taxa and microbial metabolites exhibit altered levels in MDD individuals compared to healthy individuals and to establish mechanistic links between the intestinal microenvironment and neuroinflammation in patients with MDD. For this reason, we propose a pilot multimodal study that will leverage on an ongoing NIH-funded clinical trial measuring NI in patients with MDD by obtaining repeat positron emission tomography (PET) imaging before and after an eight-week course of celecoxib (a Cox-2 inhibitor), which is led by Drs. Parsey and DeLorenzo. In Aim 1, we propose to additionally collect and perform microbial and metabolomics profiling in longitudinal fecal and blood samples in the ongoing clinical trial led by Drs. Parsey and DeLorenzo. These samples will be collected when the participants in this clinical trial are scheduled to undergo repeat PET brain imaging before and after treatment with celecoxib. Because multiple studies report overlap between psychiatric illness such as MDD and functional GI disorders, in Aim 2, we propose to also phenotype participants with respect to functional GI disorders which are known to be mediated by the gut-brain axis. It is possible that the patients with functional GI disorders and MDD represent a subgroup of MDD that may be more responsive to manipulation of the microbiome compared to individuals with MDD who do not have functional GI disorders. To analyze the microbial composition and microbial derived metabolites, Dr. Aroniadis has assembled a multidisciplinary team that takes advantage of multiple research core services (e.g. Biostatistical Consulting Core, Mass Spectrometry Core, GI Clinical Translational Core) at Stony Brook University. We anticipate that this project will strengthen the research program on the role of the human microbiome in health and disease at this institution. The preliminary sample collection and data analysis over 12 months will be used in submitting an NIH R01 led by Dr. Aroniadis, an early stage investigator, and her colleagues, Drs. Parsey and DeLorenzo, highlighting a novel multimodal approach towards probing the role of the gut microbiome in mediating signaling along the gut-brain axis in MDD.