FECAL MICROBIOTA TRANSFER WITH STOOL FROM HUMAN IBD PATIENTS RESULTS IN NEUROINFLAMMATION AND ANXIETY-LIKE BEHAVIOR IN MICE

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Introduction

16s RNA Sequencing

Inflammatory bowel disease (IBD) is a term that describes two disorders involving chronic inflammation of the gastrointestinal tract— Chron's Disease (CD) and Ulcerative Colitis (UC). Patients with IBD have a markedly increased incidence of anxiety and depression disorders resulting in loss in quality of life as well as complicating the clinical management of IBD. Our prior data demonstrates that restoring a normal gut microbial community structure attenuates neurocognitive loss in models of brain injury and aging.

Hypothesis

We hypothesized that an IBD-associated gut microbial community structure would induce neuroinflammation and an anxiety-like phenotype in mice.



1. The large gray portion refers to low abundance genera which indicates high diversity in the healthy control slurry samples as compared to the IBD slurry. The IBD slurry shows higher abundancies of Parabacteroides, E. Shigella and Bacteroides which are associated with IBD related dysbiosis as well as mucosal immune activation and inflammation.

Methods



IL10 Cytokine Analysis



2. IBD slurry had much lower levels of IL-10 in their brains compared to healthy control slurry treated mice and the vehicle treated mice (*p<.05 and **p<.003). This drop in IL-10 might be a sign that the brain's immune environment is being thrown off balance. Since IL-10 helps control inflammation, having too little of it in the brain could make it more vulnerable to damage from an overactive immune response.

Neurocognitive Behavior

Figure 3. Zero Maze Tracings





 Tracings of mice in the Zero Maze behavior test revealed a reluctance of mice given IBD slurry to explore the open space concluding abnormally high levels of anxiety when compared to Healthy Control treated and PBS vehicle treated groups.

4. This is %time spent in open areas of the Zero Maze. Mice given healthy control (HC) and PBS vehicle spent comparable % time in the open areas of the maze while mice treated with IBD spent significantly less time in the open areas of the zero maze concluding abnormally high levels of anxiety (*p<.01 and **p<.002).

Conclusions

- FMT from IBD patients with an active disease flare induces anxiety like behaviors and neuroinflammation in mice.
- Look further into the alterations in gut microbiota as well as identifying specific taxa or metabolites
- Test whether probiotics or targeted antibiotics can reverse or prevent the behavioral and inflammatory effects seen in IBD

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