1. Introduction

The gut microbiota is a complex metabolic ecosystem, which interacts with the host via immunological, neuroendocrine and neural pathways. These pathways are integral components of the brain-gut-microbiota axis and preclinical evidence suggests that the microbiota can recruit this bidirectional communication system to modulate brain development, function and behaviour [1]. Although it is well acknowledged that the pathophysiology of depression involves immunneuro-endocrine dysregulation [2][3] the extent to which changes in the gut microbiota composition and function mediate dysregulation of these pathways in depression is currently unknown.

2. Aims

1. To determine the composition, richness and diversity of the gut microbiota in Depressed patients compared to healthy control participants and its relationship to: Short Chain Fatty acids (SCFAs), Immune activity (plasma cytokines), Hypothalamic-Pituitary-adrenal axis (HPA-axis) function and Tryptophan metabolism

2. To determine the behavioural & physiological effects of a Fecal Microbiota Transplantation from Depressed patients & health controls to a microbiota depleted antibiotic rat model

3. Methods

Study Population: 34 patients with DSM IV MDD & 33 healthy subjects matched for gender, age & ethnicity.[see Table 1 for demographics and clinical characteristics]

Measures:

Gut Microbiota Structure & Diversity: 16s rRNA gene sequencing

Microbial Metabolites: Outlier than fatty acids (Gut Chromatograph)

Hypothalamic-Pituitary-Adrenal (HPA) Axis: Salivary Cortisol (BISAS)

Inflammation: plasma Cytokines & CRP (Meso Scale Discovery)

Tryptophan Metabolites: Plasma Kynurenine & Lactobacillus (HPLC)

Intestinal Permeability: plasma Lactobacillus Binding Protein

Subjective Mood & Stress: Hamilton Depression Rating Scale (HAM-D), Beck Depression & Anxiety scales (BDI & BAI), Perceived Stress scale (PSS), Pittsburgh Sleep Quality Index (PSQI)

Diet & Exercise: Food Frequency Questionnaire (FFQ), International Physical Activity Questionnaire (IPAQ)

Rats: 28 Male Sprague-Dawley rats

Behavioural tests: Sucrose preference (SP), Open field (OF), Elevated plus maze (EPM), Intertemporal mobility (IM), Forced swim test (FST), Inescapable-based (IBS) (once a week)

Physiological outputs:

HPA-Axis: Cortisol levels 60 mins post FST

Inflammation: plasma Cytokines & CRP

Tryptophan Metabolites: plasma Tryptophan & Lactobacillus (HPLC)

Intestinal Permeability: plasma Lactobacillus Binding Protein

Intestinal Motility: Transit Time

4. Subject Demographics

5. Results

Altered Inflammatory & Tryptophan Metabolite Profile in Depression

Altered Gut Microbiota Composition, Diversity & Richness in Depression

6. Conclusions

Our results confirm that depression is associated with a distinct microbial signature which is capable of inducing alterations in behaviour and physiology when transferred to microbiota-depleted animals. This suggests that the gut microbiota may play a causal role in the development of core behavioural and neurobiological features of depression and may provide a tractable target in the treatment and prevention of depression.

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