A261

MICROBIOTA PROFILES OF PATIENTS WITH MENTAL DISODERS DIFFER FROM THOSE OF HEALTHY CONTROLS.

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Background: Mental disorders are the leading cause of disabilities worldwide, with depression and anxiety among the most common ones, affecting up to 1/3 of the worldwide population at least once in their lifetime. In both preclinical models and clinical studies, gut microbiota has been associated with altered behavior and anxiety or depression, respectively.
Aims: To investigate 1) whether the microbial profiles of patients with generalized anxiety disorder (GAD) and major depression disorder (MDD) differ from those of healthy controls (HC), and 2) whether specific bacterial taxa associate with GAD or MDD.
Methods: 118 patients with primary GAD (n=82, 83.3 % female) or MDD (n=36, 62.9 % female) and 99 matched HC (66.6 % female) were recruited through the Anxiety Treatment and Research Centre. Anxiety, depression and stress levels were assessed by DASS-21 questionnaire. Stool samples were collected anaerobically and analysed for 16S rRNA gene sequencing through Illumina technique. The data was divided in 4 groups: 1) mental health disorder (MHD) combining GAD and MDD, 2) GAD, 3) MDD, and 4) HC. The data was analyzed following the pipelines of dada2 and QIIME2. RandomForest plugin for QIIME2 was used to investigate predictive characteristics of MHD, GAD or MDD microbiota. SPSS software v.23 was used to perform Spearman correlations and logistic regressions between microbial taxa and clinical scores.
Results: The mean anxiety score was 16.2 (severe anxiety) for GAD patients and 9.8 (moderate anxiety) for MDD patients; the mean depression score was 19.2 (moderate depression) for MDD patients and 16.0 (moderate depression) for GAD patients, while healthy controls averaged only 1.5 (normal anxiety) and 1.7 (normal depression) for anxiety and depression, respectively. The microbiota profile of the MHD group was predictive of the patients' disease state with an 83.3% accuracy. In particular, increased relative abundance of *Bacteroides ovatus* and *Bacteroides* spp. and decreased relative abundance of *Dialister* spp. (Veilonellaceae), *Haemophilus parainfluenzae* and *Bifidobacterium adolescentis*, were predictive of MHD. Neither

the GAD or MDD group microbiota profiles alone were accurate in the prediction of the patients' disease state. There was a positive correlation between the relative abundance of *Bacteroides* spp. and a negative correlation between the relative abundance of *Clostridium sensu stricto* spp. and *Sutterella*, and the clinical scores of combined MDH and HC groups.
Conclusions: Our data suggest that patients with mental health disorders have different microbiota profiles compared to healthy controls. We have identified specific bacterial signatures that will inform mechanistic studies in gnotobiotic mouse models to investigate further the role of microbiome in mental disorders.

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