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Persons With Schizophrenia Exhibit Altered Gut Microbiome Functional Pathways Related to Immune Modulation and Cardiovascular Risk

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Background: Persons with schizophrenia have higher rates of cardiovascular disease and exhibit inflammatory abnormalities. Emerging evidence has linked the gut microbiome changes to schizophrenia. However, there has been limited research into the functional pathways by which the gut microbiota contributes to the phenotype of persons with chronic schizophrenia.
Methods: We characterized the composition and functional potential of the gut microbiota in 48 individuals with chronic schizophrenia and 48 matched non-psychiatric comparison subjects (NCs) using 16S rRNA sequencing. PICRUSt was performed to predict functional potential of microbial communities, based on metagenomes inferred from 16S data.
Results: Patients with schizophrenia demonstrated significant beta-diversity differences in microbial composition ($p=0.002$) and predicted genetic functional potential ($p=0.008$), compared to NCs. Alpha-diversity of taxa and functional pathways were not different between groups. Random forests analyses revealed that the microbiome predicts differentiation of patients with schizophrenia from NCs using taxa (75% accuracy) and functional profiles (67-70% accuracy). Differential abundance testing revealed that the family Lachnospiraceae was associated with schizophrenia ($p=0.005$). Functional pathways related to trimethylamine-N-oxide reductase and Kdo2-lipid A biosynthesis were altered in schizophrenia ($p<0.001$). These metabolic pathways were correlated with higher Framingham Risk Score ($\rho=0.393$, $p=0.026$) and decreased levels of anti-inflammatory cytokine IL-10 ($\rho=-0.761$, $p=0.001$), respectively, in patients with schizophrenia.
Conclusions: Findings suggest potential mechanisms by which the microbiota may impact the pathophysiology of the disease through modulation of functional pathways related to immune signaling/response and lipid and glucose regulation, which might have implications for accelerated biological aging in schizophrenia.
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Keywords: Microbiome-Gut-Brain Axis, Schizophrenia, Accelerated Aging, Cardiovascular Disease, Inflammation

mGluR5 Availability in Chronic Pain: An in Vivo Study With [18F]FPEB PET Study

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Background: Chronic pain (CP) is frequently treated with opioid-based analgesics leading to high rates of addiction. Identification of novel targets to rapidly reduce pain in CP without leading to substance misuse must be prioritized. Using positron emission tomography (PET) we conducted a novel examination of the role of mGluR5 - a potential treatment target for CP with low abuse-potential - in chronic pain and cognitive deficits in individuals reporting CP and those with no pain (NCP).
Methods: Participants (n=25 CP [MAge=36.76, 13 female, 16 MDD or PTSD]; n=25 NCP [MAge=38.08, 13 female, 16 MDD or PTSD]) were matched for age, gender, diagnostic and smoking status. Participants completed 1 MRI and 18F-FPEB PET scan, psychiatric and cognitive assessments.
Results: MANOVA analysis showed significant group differences in mGluR5 availability (VT; $F=4.91$, $p=.001$). CP individuals had significantly higher mGluR5 availability in frontal (p's=.001-.004, 16-21% difference) regions. Results remained significant when mood symptoms and psychiatric diagnosis were controlled for (p's=.001). ACC mGluR5 availability was higher in females ($p=.04$, 13% difference) with CP compared to ??. mGluR5 availability was negatively correlated with attention (r's=.-45-.50; p's=.02-.03), and working memory (r's=-.48-.57; p's=.007-.04) in CP.
Conclusions: Individuals with CP had higher mGluR5 availability in frontal regions, with ACC mGluR5 particularly high in females. This gives support to animal work showing dysregulation in mGluR5 in pain models. Additionally, the negative association between mGluR5 and attention (most identified cognitive dysregulation on CP) suggests targeting this receptor may provide some cognitive restoration. Further evaluation of mGluR5 targets for the treatment of chronic pain is warranted.
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Keywords: Chronic Pain, mGluR5, PET Imaging, Sex Differences

Shared Genetic Effects may Partially Explain Higher Depression and PTSD Prevalence Among Women Using Hormone Therapy (HT)

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Background: Fluctuating gonadal hormone levels are thought to contribute to the higher prevalence of major