receptor is the HPA axis response to stress. Hypothalamic corticotropin-releasing hormone (CRH) neurons, which affects glucocorticoid release by stimulating pituitary adrenocorticotropin (ACTH) secretion, are directly and indirectly inhibited by β-endorphin-producing neurons via the μ opioid receptor (OPRM). Both exaggerated and blunted HPA responses to stress have been associated with high risk for psychosis. Many studies have suggested that opioids play an important role in response to stress, motivation, and numerous psychiatric entities. The present association study tested the hypothesis that the Asn40Asp substitution polymorphism confers susceptibility to schizophrenia.
Methods: After informed consent was obtained, 100 schizophrenia patients and 100 control subjects were enrolled in this study. Genomic DNAs were extracted from peripheral blood by using the modified SDS/Proteinase K procedure. The genotypes of the Asn40Asp polymorphism of the μ opioid receptor were assessed by allele-specific polymerase - chain reaction. The PCR products were digested by restricted enzyme.
Results: The frequency of the Asp40 allele was significantly increased in all schizophrenia patients (Fisher's Exact Test P= 0.0118). There were no associations the Asn40Asp polymorphism of the μ opioid receptor with substance dependence among schizophrenia patients and normal control.
Discussion: The opioidergic neurotransmitter system plays an important role in regulating activation of the hypothalamic-pituitary-adrenal (HPA) axis. Initial activation of the HPA axis occurs at the level of the paraventricular nucleus of the hypothalamus, where neurons that produce corticotropin releasing factor (CRF) are located [Bell et al., 1998]. CRF neurons in this area express μ-opioid receptors and are under tonic inhibition by neurons of the arcuate nucleus that contains β-endorphin [Wand et al., 1998]. Genetic factors appear to be important modulators of HPA axis activation. The HPA axis appears to be involved, including the normal stress response [Bond et al., 1998; LaForge et al., 2000] and psychosis in which HPA axis dynamics appear to be abnormal. Similarly, there is growing evidence that altered opioidergic neurotransmission and HPA axis dynamics may affect alcohol- and drug-seeking behaviors [Piazza and Le Moal, 1997; Kreek and Koob, 1998].

T191. RANDOMIZED DOUBLE-BLIND FEASIBILITY STUDY OF A GLUTEN-FREE DIET IN PEOPLE WITH SCHIZOPHRENIA AND ELEVATED ANTIGLIADIN ANTIBODIES (AGA IGG)

Deanna Kelly*[,1], Haley Demyanovich[1], Katrina Rodriguez[2], Daniela Cihakova[2], Monica Talor[2], James Gold[1], Sharon August[1], Robert Buchanan[1], Stephanie Feldman[1], Fang Liu[1], William Carpenter[1], William Eaton[2]
[1]University of Maryland Baltimore, Maryland Psychiatric Research Center; [2]Johns Hopkins Bloomberg School of Public Health

Background: Deconstructing schizophrenia is important, since different disorders within the syndrome may have distinct pathophysiological mechanisms and treatment targets. Emerging evidence suggests inflammation may play a role in at least a subgroup of people with this illness. One specific subgroup with known inflammation is a group with elevations in antigliadin antibodies (AGA IgG). These elevations (>20 U) are found in about 1/3 of people with schizophrenia. Gliadin is a protein found in wheat, barley and rye. This subgroup with AGA IgG elevations may be distinct as they have fewer positive symptoms, higher kynurenic acid levels, and may benefit from a gluten free diet. The effectiveness of gluten removal has been controversial with mixed results in previous studies, however no former study has examined gluten removal in those with high AGA IgG, that is, the population who may be expected to benefit.
Methods: Sixteen people with a DSM-IV-TR diagnosis of schizophrenia or schizoaffective disorder and who also had elevated AGA IgG (≥20 U) were recruited and admitted to an inpatient unit for a 5-week randomized double blind trial. Participants were randomized in a double blind fashion to either a diet containing gluten or a complete strictly enforced gluten free diet. This was accomplished by given 10 gm of gluten flour or 10 gm of rice flour daily in a protein shake, with all meals for all participants being standardized and gluten free. Participants had cooking classes, received cookbooks, and went on shopping trips for gluten free foods and meals. Participants were rated on the Brief Psychiatric Rating Scale (BPRS), Scale for the Assessment of Negative Symptoms (SANS) and the MATRICS Cognitive Battery (MCCB) at baseline and 5 weeks. The study was not powered to find a treatment effect, but designed to examine the feasibility of conducting an inpatient gluten removal study and examine trends in treatment as measured by Cohen's D effect size (ES) differences.
Results: Fourteen of 16 people completed the 5-week trial and all tolerated the diet (2 discontinued early in the trial for housing and administrative reasons). The mean age of participants was 37.9 ± 13.2 years, 56% male and 75% African-American. During the clinical trial, participants receiving the gluten free diet had an improvement in negative symptoms as compared to placebo (treatment difference) with an ES=0.53. There was no improvement in BPRS total score or positive symptoms. The MCCB composite score did not improve, but an ES=0.6 was noted in the domain of attention favoring the gluten free diet. The AGA IgG levels decreased by 35% in the five weeks in the gluten free diet group relative to a 17% decrease in the gluten containing group. It is also important to note that the correlation between the change in SANS total score and AGA IgG in the gluten free group (r=0.57) was strong and notably different than the correlation between the change in SANS total score and AGA IgG in the gluten containing group (r=-0.017), suggesting a possible marker of treatment effect. Adverse effects were similar between treatment groups.
Discussion: This is the very first study of a gluten free diet in schizophrenia with elevated AGA IgG. This feasibility study suggests that removal of gluten is associated with improvement in negative symptoms and attention, but not positive symptoms. Participants tolerated the diet. The feasibility study provided data to design the now ongoing fully powered confirmatory double-blind trial in people with schizophrenia with negative symptoms using a higher gluten amount (30 grams daily) and with aims to examine associated mechanisms, with targets of inflammation, neuroimaging and gut permeability.

T192. THE GUT MICROBIOME IN SCHIZOPHRENIA AND ANTIPSYCHOTIC INDUCED METABOLIC DYSFUNCTION

Sarah Kanji[1], Ilona Gorbovskaya[1], Trehani Fonseka[1], Kazunari Yoshida[1], Victoria Marshe[1], Malgorzata MacKenzie[1], Premysl Bercik[2], Elena Verdu[2], Margaret Hahn[1], Daniel Mueller*[,3]
[1]Centre for Addiction and Mental Health; [2]McMaster University; [3]University of Toronto

Background: Antipsychotic (AP) medications are the cornerstone of treatment for schizophrenia (SCZ), with off-label prescription rapidly increasing in youth and adolescent populations. However, APs have been associated with metabolic side effects including diabetes and obesity. Although several mechanisms have been proposed, the gut microbiome (GMB) has been suggested as a potential mediator of AP-induced metabolic side effects due to its role in weight and metabolic regulation; as well as emerging evidence demonstrating a shift in the microbiome of AP-treated animals and humans. The purpose of the current study is to 1) Investigate the GMB in SCZ patients compared to healthy individuals and 2) To examine the role of GMB in SCZ and AP-induced metabolic side effects.
Methods: Three groups of 25 participants are being recruited. Group A: Long-term AP-treated patients (for at least 6 months) taking clozapine (CLZ). Group B: Healthy controls matched with Group A for BMI, age, sex, and smoking status. Group C: Treatment-naive SCZ patients