Poster Session II

F1. GENOME-WIDE ASSOCIATION STUDIES SUGGESTED ASSOCIATION BETWEEN DGKB AND ANTIPSYCHOTIC INDUCED WEIGHT GAIN IN EUROPEANS AND AFRICAN AMERICANS

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Background: Schizophrenia (SCZ) is a severe, devastating disorder with a life-time prevalence of 1% irrespective of gender or ethnic group, treated primarily with antipsychotic (AP) medications. Despite clinical efficacy of APs, they are associated with severe side effects including antipsychotic-induced weight gain (AIWG).
Methods: We investigated n=201 schizophrenia or schizoaffective disorder patients of European and African American ancestry who were treated mostly with clozapine or olanzapine. Individuals were genotyped on the Infinium Omni2.5 BeadChip. We conducted genome-wide association analysis for AIWG defined primarily as the percentage of weight change from baseline. Additionally, we ran pathway, enrichment, network, and polygenic risk score analyses to investigate top genes using in silico methods.
Results: In the mixed sample, we observed genome-wide significant association between the diacylglycerol kinase beta (DGKB) variant (β=0.411; p=3.15 × 10–9) and percentage of weight change. The association remained nominally significant in both Europeans (β=0.271; p=0.002) and African Americans (β=0.579; p=5.73 × 10–5) for the same risk allele. In Europeans, the top variant (β=0.406; p=1.26 × 10–6) was located upstream of the Stanniocalcin 2 (STC2) gene. Bayesian fine mapping suggested the variant nearby SNP upstream of STC2 (p=0.034; PHRED=3.691, posterior prob.=0.496) to be the most significant. We noticed no significant enrichment in metabolic pathways for SNPs, but our top genes (p<5 × 10–5) were enriched in the GWAS catalog for risk of obesity (pmixed=0.018; pEuropeans=0.015) and schizophrenia (pmixed=0.006). Top genes also interacted with known risk factors for obesity (Glucose-6-Phosphate Dehydrogenase (G6PD)) and schizophrenia (NudE Neurodevelopment Protein 1 Like 1 (NDEL1)), and are targeted by microRNAs related to schizophrenia (mir-34a) and obesity (mir-19b). Polygenic risk score analyses did not provide support for major genetic overlap between obesity-related and lipid-associated SNPs and the risk of AIWG.
Discussion: Our findings suggested that a variant in DGKB is associated with the percentage of weight gain in both African Americans and Europeans.

F2. CHILDHOOD TRAUMA AND LACK OF CULTURAL IDENTITY AS RISK FACTORS OF ATTENUATED PSYCHOSIS SYMPTOMS AMONG AFRICAN AMERICAN YOUNG ADULTS

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Background: Schizophrenia spectrum diagnosis is more commonly assigned to African Americans. Failing to understand and appropriately manage cultural differences will have significant mental health consequences for varied racial/ethnic groups in particular (Betancourt, Green, & Carrillo, 2002). The purpose of the present study was to examine risk factors of attenuated psychosis syndrome in a sample of African American young adults, specifically to investigate whether lack of ethnic identity and adverse childhood experiences (ACEs) put an individual at a higher risk of developing attenuated psychotic symptoms.
Adverse Childhood Experiences (ACE) as Risk Factor of APS:
The Comorbidity Survey (NCS) Part 2 data showed that the effects of neglect and sexual abuse, along with physical abuse similarly put a child at risk for psychosis. People who had suffered childhood adversity were 2.8 times more likely to develop psychosis than those who had not. Studies have also begun to look at gender differences in schizophrenia by way of ACEs.
Lack of Ethnic Identity as Risk Factors of APS:
The African worldview reflects psychological communal, spiritual, collective survival thrust as opposed to the European worldview of individualism and materialism. Cultural Misorientation (CM) represents that foreign psychological or psychopathological disposition in the African personality, which allows African Americans to unknowingly value and participate in European cultural indoctrination through the practice of European cultural values, rituals, and customs. The purpose of this study was to explore the roles that CM play on the overall presentation of attenuated psychotic symptoms, by way of ACE exposure.
Methods: Participants: Participants included 304 African American college students, 199 (65.46%) women and 105 (34.54%) men from a Historically Black College and University in the southeastern region of the United States. Participants were between 18 and 25 years of age.
Instruments: Adverse Childhood Experiences Scale measures the association of multiple types of abuse with different types of health outcomes. Prodromal Questionnaire- Brief (PQ-B) measures the presence of negative symptoms, perceptual abnormalities such as hallucinations, and unusual thought content like delusional ideas and paranoia. Cultural Misorientation - Short Form assesses the condition of cultural misorientation across 6 subscales-- materialism orientation, individualism orientation, alien-self orientation, anti-self orientation, self-destructive orientation, and integration orientation.
Results: The Pearson correlation analysis indicated no significant relationship (r = -.073, p = .206) between ACE exposure and APS total scores on PQ-B. However, an unexpected negative significant relationship between childhood abuse exposures and symptom severity was observed (r = -.126*, p = .028), indicating that participants who reported more instances of childhood abuse tended to report less symptom severity. In addition, Cultural Misorientation (CM) was significantly positively correlated to PBQ total scores r = .194**, p = .001) and the severity of those symptoms (r = .171**, p = .003). CM materialism and individualism subscales mediated the relationship between childhood abuse and PQ-B total scores and symptom severity.
Discussion: This study provides support that some aspects of cultural misorientation can be detrimental to African Americans. Helping to reduce material and individualistic desires that have become detrimental should also be a central focus of implemented mental health programs.

F3. A CASE OF LEUKOCYTOSIS ASSOCIATED WITH CLOZAPINE TREATMENT FOR THE MANAGEMENT OF CHRONIC SCHIZOPHRENIA

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Background: Clozapine is an atypical antipsychotic drug with therapeutic efficacy through serotonin-dopamine antagonism. It has been used for the management of treatment-resistant schizophrenia and reducing the risk of suicidal behavior. In addition to agranulocytosis and leukopenia, clozapine has also been reported to be associated with other types of blood dyscrasias, including leukocytosis.
We wish to report a case of leukocytosis associated with clozapine treatment in a patient of chronic schizophrenia.
Methods: Our patient is a 48-year-old woman with a diagnosis of schizophrenia since the age of 22. She has a history of numerous hospitalizations and substantial treatment with conservative antipsychotics.
We evaluated her medical and psychiatric history as well as mental status. Then We assumed that she might have treatment-resistant schizophrenia and accordingly commenced treatment with clozapine. At the time of admission, her WBC count was 8.01 × 109/L and ANC was 5110. Clozapine was started at 3rd hospital day. We stopped aripiprazole and gradually increased clozapine. Only 2mg of lorazepam was used in combination with clozapine. Remission was achieved with 450 mg/day of clozapine. WBC on the 1st day of treatment was 12.41 × 109/L (ANC; 9481) and clozapine was 300mg/day. WBC on the 18th day of treatment was 15.32 × 109/L (ANC; 12501), and at that time, her clozapine dosage was 450mg/day. At this point, her vital sign was within normal range and physical examination did not showed any infectious signs. On the 25th day of treatment, WBC count was 22.1 × 109/L and ANC was 17680. However, no general medical condition to explain the leukocytosis was found.
We concluded that her leukocytosis was linked to clozapine, and decided to taper out clozapine despite there being no medical contraindication. After two weeks from starting blonanserin and olanzapine, WBC count normalized. Fortunately, despite replacing the medication, the remission was maintained.
Results: In our case, the increase in white blood cell count with increasing dose of clozapine was evident and did not reveal any other medical cause to explain leukocytosis in the patient. In addition, leukocytosis improved significantly after discontinuing clozapine. Also, there have been reports of cases of leukocytosis associated with clozapine treatment, and the mechanism of leukocytosis has been explained to some extent. Considering these temporal associations, mechanisms, and previous cases, it is reasonable to consider leukocytosis associated with clozapine in this case.
Discussion: This case suggests a temporal relationship between the use of clozapine and leukocytosis. It also shows the rapid resolution of leukocytosis after discontinuation of clozapine. The mechanisms of clozapine-induced leukocytosis may be related to changes in plasmatic concentrations of granulocyte colony-stimulating factor, tumor necrosis factor-α, interleukin (IL)-2 and IL-6 cytokines, which could be stimulated by clozapine. In our case, an increase in WBC count was consistent with an increase in clozapine dose, suggesting a dose-dependent effect. However, the appearance of leukocytosis during clozapine treatment does not mean that clozapine should be discontinued. Nevertheless, the WBC continued to increase steadily, and clinicians inevitably replaced the drugs in consideration of the fact that he was not a general hospital but a psychiatric clinic.
In this paper we have reported a patient of chronic schizophrenia who developed leukocytosis during clozapine treatment. It appears that most of clozapine-associated leukocytosis can be benign medical condition. However, clinicians should be aware of the dangers of other blood disorders such as leukocytosis.

F4. LINKING LIFE EVENTS WITH NEGATIVE AFFECT AND PSYCHOTIC EXPERIENCES IN DAILY LIVES OF YOUTH: STRESS SENSITIVITY AS A PUTATIVE MECHANISM?

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Background: Negative life events are associated with a range of mental disorders, including psychosis. However, evidence on underlying mechanisms remain scarce. The current study aimed to investigate whether life events (e.g. intrusive threat, experience of loss, illness) impact on the sensitivity towards stress in daily lives of youth.
Methods: The Experience Sampling Method was used to measure momentary stress (i.e. event-related, activity-related, social), negative affect, and psychotic experiences in a sample of 42 help-seeking adolescents and young adults (service user), 17 siblings, and 40 comparison subjects (controls). Life events during lifetime and the previous year as well as depressive, anxiety, and psychotic symptoms were assessed.
Results: Stress sensitivity, that is, the associations between momentary stress and (i) negative affect and (ii) psychotic experiences, was modified by lifetime and previous negative life events in service users. While there was strong evidence for increased negative affect and psychotic experiences in service users when high vs. low levels of lifetime exposure to negative life events were compared a pattern of resilience was evident in controls with no marked differences in the magnitude of associations comparing high vs. low exposure levels. However, in controls, exposure to life events during the previous year were also found to impact on the stress sensitivity in daily life. Less consistent findings were observed in siblings.
Discussion: Our findings point to the importance of time that has passed between exposure to and impact of life events on stress sensitivity: while the detrimental effects may attenuate in controls over time, service users appeared to be at greater risk of negative long-term effects. Thus, stress sensitivity may constitute an important risk and resilience mechanism through which adverse life events impact on mental health in youth. Targeting stress sensitivity in daily life through ecological momentary interventions, potentially with stronger effects shortly after stress exposure, may represent a promising novel therapeutic approach.

F5. CLOZAPINE RELATED THROMBOCYTOSIS AND THROMBOCYTOPENIA

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Background: It is well known that clozapine causes hematological side effects such as agranulocytosis, neutropenia, and leukocytosis. But, the results about the effects of clozapine on the number of platelets were not consistent. Although thrombocytopenia or agranulocytosis are regarded as more clinically important side effects, thrombocytosis should be monitored because it may be related with increased the risk of thrombosis and pulmonary embolism. We investigated the effect of clozapine on the number of platelets in schizophrenia patients starting clozapine.
Methods: This was a retrospective chart review study using ABLE, an electrical medical record inquiry system of Asan Medical Center. Among individuals who were diagnosed schizophrenia, who applied clozapine more than three months were included as study subjects. Those who were unable to identify the complete blood count (CBC) at the beginning of the clozapine administration and who did not perform more than one CBC at least every 3 months during the observation period were excluded from the study. CBC scores at baseline and at 1, 3, 6, 9, and 12 months after the initiation of medication were obtained, and the mean platelet counts at the initiation and platelet counts at each observation period were compared by paired t-test. The cumulative incidence of thrombocytopenia (<150000 / mm3) and thrombocytosis (> 450000 / mm3) for one year were also calculated.
Results: Ninety-six patients were enrolled in this study and 50 and 41 subjects were remained at month 6 and 12, retrospectively. There was a significant mean platelet change only at month 1 (275.292 ± 74.464/mL) compared to the initiation of treatment (255.500 ± 74.464/mL) (t=-3.553, p>0.001). The cumulative incidence rates were 3.13% for thrombocytopenia, 6.25% for thrombocytosis.