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Background: Individuals at ultra-high-risk for psychosis (UHR) are characterized by decline in cognitive functions. As cognition are suggested to be structural dependent on cerebral white matter organization, we here examine, if patterns of cognitive functions are associated with alterations in white matter for UHR compared to healthy controls (HC).

Methods: 116 UHR and 49 HCs underwent diffusion weighted imaging using a 3 Tesla magnetic resonance imaging scanner and were cognitively assessed. Group differences on whole brain fractional anisotropy were tested using tract-based spatial statistics. With univariate general linear modelling we tested group differences on cognition and white matter fractional anisotropy, voxel-wise and in regions of interest. Using multivariate testing, we examined associations between patterns of cognitive functions and regional fractional anisotropy. Finally, we tested covariance between the patterns of cognitive functions and additional white matter measures.

Results: As expected for UHR, we found significant impairments on 14 out of 17 outcomes for cognitive functions, and lower fractional anisotropy in one focal cluster comprising the superior longitudinal fasciculus R and cingulum (cingulate gyrus) R. Multivariate analyses indicated different associations between patterns of cognitive functions and white matter microstructure for UHR compared to HCs. Significant correlations between similar cognitive function and different regional fractional anisotropy patterns in UHR compared to HCs (omnibus test $p=0.038$) was revealed. Two strongly significant covariations were identified: LV5 ($p=0.002$) explaining 7.4% of the covariance; and LV6 ($p=0.011$) explaining 5.5% of the covariance. Patterns of cognitive functions were associated with interaction effect on fractional anisotropy in localized regions: fornix and medial lemniscus bilateral (LV5), and uncinate fasciculus L and superior Cerebellar Peduncle L (LV6). Analyses of additional white matter measures suggested dysmyelination as partly underlying the unique covariation between cognition and white matter microstructure for UHR.

Discussion: The localization of the white matter abnormalities is in accordance with previous studies identifying superior longitudinal fasciculus and cingulum with altered white matter microstructure in patients with schizophrenia and affective disorders. The unique associations between specific patterns of cognitive functions and regional interaction-effects on fractional anisotropy, suggest that the underlying structural basis for cognitive function is different for UHR compared to HCs. The analysis of covariance on additional white matter measures suggested dysmyelination to be partly explanatory.

T98. LATENT IRON DEFICIENCY AS A MARKER OF NEGATIVE SYMPTOMS IN PATIENTS WITH FIRST-EPISEDE SCHIZOPHRENIA SPECTRUM DISORDER

Abstract not included.

T99. AUDITORY PROCESSING DEFICITS IN RODENTS WITH A SCHIZOPHRENIA ASSOCIATED MUTATION IN KALIRIN

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Background: Deficits in auditory processing are seen in patients with schizophrenia. Evidence implicates altered auditory cortical dendritic

developments, such as reduced dendritic arborization, contribute to these symptoms. Increased Kalirin, a protein critical in dendritic morphogenesis, is seen in postmortem auditory cortical samples of patients with schizophrenia, and the resulting impaired signaling is thought to contribute to functional deficits. Our group recently established that a missense gain of function mutation in the Kalirin gene, P2255T (KAL-PT), leads to decreased auditory cortical dendritic length and complexity in 12-, but not 4-week old mice. However, it is unclear whether these contribute to auditory sensory impairments. Here, using the gap-induced pre-pulse inhibition of startle response test (gap-PPI), we examined whether KAL-PT mice exhibit behavioral deficits compared to wild-type animals (WT), and whether the deficits are specific to the auditory domain.

Methods: 4- and 12-week old mice were tested for gap-PPI through insertion of silent gaps (1, 2, 4, 7, 10, 20, 40, 100, and 250 ms) within a 70 dB white noise prior to the presentation of a 105 dB startle stimulus. Startle response was defined as the maximum force applied by the mouse to the apparatus. Data were analyzed using factorial repeated measures analysis of variance with genotype as between-subject factors and gap duration as within-subject factors. One-sample t-tests for each gap duration were analyzed for PPI above threshold (i.e. 0%). Data were expressed as mean \pm SD, and $p < 0.05$ was considered statistically significant.

Results: Surprisingly, results indicated a significant main effect of genotype in the 4- ($p=0.049$), but not 12-week old mice ($p=0.651$). One-sample t-tests demonstrated 4-week old WT were able to discriminate the gap stimulus at 10 ms ($p=0.020$), whereas 4-week KAL-PT detected gap at 40 ms ($p=0.017$). For 12-week old animals WT were able to discriminate the gap stimulus at 7 ms ($p=0.031$), while KAL-PT detected gap at 20 ms ($p=0.011$).

Discussion: We suspect that 4-week KAL-PT may have molecular abnormalities not yet identified that led to gap PPI deficits without altering auditory cortex morphology. These alterations were either insufficient to produce long lasting impairments in auditory sensory processing, as evident in the lack of gap-PPI deficits within the 12-week KAL-PT, or possibly led to compensatory mechanisms that resulted in aberrant dendritic growth. Alternatively, the Kalirin mutation itself may drive both the behavioral deficits seen in the 4-week old animals, and the morphological changes in the 12-week old mice, via independent mechanisms, with the resulting changes in dendritic architecture normalizing gap-PPI. Clinically, our results suggest that, without additional insults, the KAL-PT mutation alone may be insufficient for the development of auditory processing deficits despite changes in neuronal morphology. Identification of functional changes within these neuronal populations may help elucidate the mechanisms by which Kalirin alters neuronal activities, and offer insights into the role this protein plays in the pathophysiology of schizophrenia.

T100. EFFECTS OF ANTIPSYCHOTIC DRUGS ON THE EPIGENETIC MODIFICATION OF BDNF GENE EXPRESSION IN THE HIPPOCAMPUS OF CHRONIC RESTRAINT-STRESSED RATS

Abstract not included.

T101. METABOLITE SIGNATURE ASSOCIATED WITH STRESS SUSCEPTIBILITY IN SOCIALLY DEFEATED MICE

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Background: Social defeat, which refers to experiences of loss during a confrontation among conspecific animals or during a hostile dispute among humans, can occur in either dyadic or group-individual encounters. Various animal models have been used to study the molecular mechanisms underpinning major depressive disorder. Among these, the social defeat paradigm has emerged as among the best approaches to evaluating depressed behavior. People frequently encounter stimuli generated by interactions with other people, and social challenges appear to be the most prevalent stressor in humans and other social animals. Furthermore, this procedure may also be considered an animal model of schizophrenia given that social defeat results in deficits in prepulse inhibition, an enhanced mesocorticolimbic dopamine response, increased phasic activity in the ventral tegmental area (VTA) dopaminergic neurons, and behavioral and neuronal cross-sensitization to amphetamines. Metabolomics is well suited for elucidating the systemic changes associated with stress because the systems underlying the stress response need to respond rapidly to threatening stimuli, and the initial events associated with the acute stress response are primarily metabolite-based. Moreover, metabolic changes have been reported in animals using a social defeat stress procedure. Specifically, the metabolism of lipids, amino acids, and energy was significantly perturbed by such a procedure. We hypothesized that measurement of the metabolomes in several key brain regions implicated in psychiatric disorders would illuminate the endogenous metabolic perturbations related to stress vulnerability and resilience, leading towards specific biomarker discovery.

Methods: Adult C57BL/6N mice were subjected social defeat stress for 10 days. Defeated mice were classified into unsusceptible (stress resilient) and susceptible (stress susceptible). Using high-resolution magic angle spinning 1H nuclear magnetic resonance (HR-MAS 1H NMR), untargeted metabolomes were measured in the amygdala (AMY), dorsal hippocampus (dHIP), dorsal striatum (dST), and prefrontal cortex (PFC).

Results: We observed perturbations of glutamine in the AMY; glutamate in the dHIP; glycine and myo-inositol in the dST; and aspartate, choline, and phosphoethanolamine in the PFC of susceptible and/or unsusceptible groups compared to the control group. The susceptible and unsusceptible groups significantly differed with regard to three metabolites: glutamine, glycine, and choline.

Discussion: To deepen our understanding of the pathophysiology of stress-related disorders, we measured metabolites in the AMY, dST, dHIP, and PFC of mice exposed to social defeat stress. Significant perturbations were observed in the metabolism of amino acids, lipids, and neurotransmitters. It was of great interest to observe that the Cho, Glu, and Gly levels of the susceptible and unsusceptible groups differed significantly. Using HR-MAS 1H NMR, we observed perturbations of Gln in the AMY, of Glu in the dHIP, of Gly and m-Ins in the dST, and of Asp, Cho, and PE in the PFCs of susceptible and/or unsusceptible groups compared with the control group. Interestingly, three metabolites, Glu, Gly, and Cho, differed significantly between susceptible and unsusceptible groups. These findings suggest that social defeat stress induces disturbances in the metabolism of amino acids, lipids, and neurotransmitters in several brain areas. Furthermore, the resulting understanding of susceptibility-related metabolites may move us a step closer to elucidating the factors underpinning resistance to stress-related mental illnesses and identifying diagnostic biomarkers.

T102. SCHIZOPHRENIA PATIENTS AND CAREGIVERS BENEFIT FROM CULTURALLY INFORMED FAMILY THERAPY

Abstract not included.

T103. THE EFFECTS OF GROUP ARTS THERAPY BASED ON EMOTION MANAGEMENT TRAINING ON THE EMOTIONAL EXPRESSION, ALEXITHYmia, DEPRESSION AND QUALITY OF LIFE IN PATIENTS WITH SCHIZOPHRENIA

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Background: Poor emotional expression and depression of patients with schizophrenia are difficult problems in clinical situation. The objective of this study was to investigate the effects of group arts therapy based on emotion management training on emotional expression, positive emotion and negative emotion, alexithymia, depression and quality of life in patients with schizophrenia
Methods: 24 of 160 in-patients with schizophrenia, according to DSM-IV from H Mental Health Hospital, were randomly assigned to either an experimental or control group. Each group consisted of 12 patients. Group arts therapy was conducted on the experimental group twice a week, 60 minutes per session, for a total of 16 sessions, while the control group was left untreated. The following scales were used for assessment: Berkeley Expressivity Questionnaire (BEQ), Positive Affective and Negative Affect Schedule (PANAS), Toronto Alexithymia Scale-Korean version (TAS-20K), Depression Scale for Schizophrenia (K-CDSS), Positive and Negative Syndrome Scale (PANSS), and Schizophrenia Quality of Life Scale (SQLS-R4K). Independent t-test was conducted to confirm the homogeneity, and to find the effects of group arts therapy, repeated measures ANOVA was conducted to confirm the differences for scores of each scale regarding groups, measuring timing, and also the interaction between groups and measuring timing by pre, post and follow-up test.

Results: First, total score, expressivity factors and impulse strength factors of emotional expressivity were significantly increased after group arts therapy compared to the control group.

Second, positive emotion was significantly increased and negative emotion was significantly decreased after group integrative therapy compared to the control group.

Third, total score, difficulty identifying feelings of Alexithymia were significantly decreased after group arts therapy compared to the control group.

Fourth, depression was significantly decreased after group integrative arts therapy compared to the control group.

Fifth, negative syndromes and general psychopathology were significantly decreased after group arts therapy compared to the control group.

Sixth, quality of life was significantly increased after group arts therapy compared to the control group.

Discussion: The group arts therapy has significantly improved the emotional expression, positive emotion, negative emotion and Alexithymia in patients with schizophrenia and also improved negative syndromes, general psychopathology, depression and quality of life. These results suggest that group arts therapy based on emotion management training could be a useful intervention for emotional disturbance treatment for in patients with schizophrenia.

T104. THE ASSOCIATION AMONG CAFFEINE INTAKE, COGNITION, AND SYMPTOMATOLOGY IN SCHIZOPHRENIA PATIENTS

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