imperations and tissue volume loss within the frontoparietal and ventral attention network, while the third clinical-anatomical phenotype encompassed a mixed positive and negative symptoms phenotype and tissue volume loss within the dorsal attention network. Critically, the pattern of volume loss within the first most prevalent clinical-anatomical phenotype mediated (a+b) the effect of socioeconomic status on clinical outcome (cognitive performance and negative symptoms) \( \text{a+b} \leq 0.033(0.088); P<1.0 \times 10^{-4}; 95\% \, \text{CI} \, [-0.049, -0.018] \). Finally, we partly replicated the first clinical-anatomical phenotype in an independent sample of patients with schizophrenia \( n=108 \).

Discussion: The heterogeneous clinical manifestation of schizophrenia can be significantly explained by three clinical-anatomical phenotypes. Despite their distributed topography, each phenotype is centered on a specific, well-defined set of intrinsic networks.

M169. HIPPOCAMPAL GLUTAMATE AND HIPPOCAMPUS SUBFIELD VOLUMES IN ANTIPSYCHOTIC-NAIVE FIRST EPISODE PSYCHOSIS SUBJECTS AND RELATIONSHIPS TO DURATION OF UNTREATED PSYCHOSIS

Abstract not included.

M170. GENETIC CHARACTERIZATION OF A COHORT OF PATIENTS AFFECTED BY SCHIZOPHRENIA. THE ROLE FOR RARE STRUCTURAL VARIANTS IN MODULATING TREATMENT RESISTANT ENDOPHENOTYPES: PRELIMINARY DATA

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Background: Schizophrenia (SCZ) is a debilitating mental illness characterized by a highly complex, heterogeneous, non-mendelian genetic background. Recent progress in dissecting genetic architecture of SCZ has accelerated over the last decade due to new advanced technologies. Genome-Wide Association Studies (GWAS) on extremely large samples has accelerated over the last decade due to new advanced technologies. The major source of integrated data is the automatized curation from MEDLINE abstract. Genome-Wide Association Studies (GWAS) on extremely large samples has accelerated over the last decade due to new advanced technologies. From this gene-disease relationship, a bipartite network of other diseases are not yet satisfactory. Genome-wide association studies have identified more than hundreds of genetic loci associated with schizophrenia. In turn, these loci are associated with a wide variety of other diseases. From this gene-disease relationship, a bipartite network can be built which, after appropriate projection, could help to map a complex disease-similarity network. In case of schizophrenia, it would reveal the position of schizophrenia among the broader categories of systemic illnesses.

Methods: DisGeNET is a discovery platform which contains one of the largest collections of gene-disease association data. The major source of the integrated data is the automatized curation from MEDLINE abstract. Therefore, it contains the timestamp of reported gene-disease association. Gene-disease-timestamp (year of publication) triplet was fed into a Neo4j graph database platform. From this, disease-disease relationships with...
shared gene count and Jaccard similarity score was extracted. The network structure of level 1.5 egocentric network centered upon schizophrenia was inspected. Louvain community detection algorithm was applied to expose underlying group structure among the 1st order alters. For comparison, similar ego-networks centered upon several major psychiatric illnesses were also inspected. Finally, the yearly variation of Jaccard score which reflected the accumulation of research data were monitored.

**Results:** The diseases which showed the highest Jaccard score (j) were bipolar disorder (j=0.203) and depressive disorder (j=0.190) as expected. Other diseases with meaningful similarity could be grouped into three communities: 1) psychiatric illness including bipolar/depressive disorder, 2) a variety of malignancies including neuroblastoma (j=0.083), stomach cancer (j=0.070) and pancreatic cancer (j=0.065) 3) other systemic illnesses including multiple sclerosis (j=0.088), metabolic syndrome (j=0.076), myocardial infarction (j=0.073), rheumatoid arthritis (j=0.070), lupus erythematosus (0.056). The gene-sharing relationship with systemic illnesses (malignancies and other) began to be revealed after 2005. Since then, more and more evidences were accumulated to solidify the schizophrenia’s link with systemic illnesses.

**Discussion:** Recently, a couple of large-scale epidemiological studies verified the significant correlation between prevalence of schizophrenia and cancer/autoimmune disorders. The present study results may augment these epidemiological data and thus strongly support the concept of schizophrenia as a systemic illness. Gene-sharing and its reflection in prevalence data would indicate deeper link at the level of pathogenesis with systemic illnesses. Recently, many authors contemplated the possible link between schizophrenia and cancer in terms of cell cycle regulation and control of apoptosis. Likewise, others suspected immunological disturbance as the fundamental mechanism of schizophrenia. In this vein, the need for extending the concept of mental disorders as a focused manifestation of systemic illness seems gaining impetus.

**M172. POLYGENIC RISK SCORES ANALYSES IN ANTIPSYCHOTIC-INDUCED WEIGHT GAIN**

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**Background:** Antipsychotic-induced weight gain (AIWG) is a common and serious side effect with antipsychotic medications, which frequently leads to obesity and metabolic disorders. Previous single-gene analyses have shown an overlap between AIWG and genes associated with obesity and energy homeostasis (e.g., MC4R). However, given the polygenic nature of AIWG, polygenic risk scores (PRSs), which combine thousands of common variants weighted by their effect size, provide a novel opportunity to investigate the genetic liability for AIWG. Therefore, we analyzed whether PRSs based on large genome-wide association studies (GWAS) for schizophrenia (SCZ), body mass index (BMI), and diabetes (Type 1 & 2) were associated with AIWG.

**Methods:** We used a combined dataset (N=345) from two cohorts, prospectively assessed for AIWG: (1) a subset of the Clinical Antipsychotic Trials in Intervention Effectiveness cohort (CATIE; n=189, Brandl et al., 2016), and (2) the Toronto multi-study cohort (n=156, Brandl et al., 2014). The combined cohort was predominantly male (n=249, 72.2%) and on average 39.3±11.9 years old with a total of 196,787 genetic variants. Our phenotypes of interest included the percentage of BMI/weight change from baseline to end-of-treatment, as well as the presence/absence of significant weight gain (≥7% weight change). We investigated associations between PRSs of SCZ, BMI, and diabetes (Type 1 & 2) and AIWG using regression models, corrected for age, sex, study duration and presence of other risk medication for AIWG. We used the Psychiatric Genomics Consortium schizophrenia GWAS reports to calculate PRSs for SCZ. We used GWAS summary statistics from the GWAS Catalog of BMI and metabolic disorders. For BMI, we used one dataset for BMI (i.e., GCST006900: 2,336,269 variants across to up to 700,000). For Type-1 diabetes (T1D), we used one dataset from the GWAS catalog (ID: GCST005536) which included 123,130 variants across 6,683 cases, 12,173 controls, 2,601 affected sibling-pair families, and 69 trios. Likewise, we used three datasets for T2D (i.e., GCST006801: 8,404,432 variants across 4,040 cases and 113,735 controls; GCST007517: 133,871 variants across up to 48,286 cases and up to 250,617 controls, and GCST007518: 133,586 variants across up to 48,286 cases and up to 250,617 controls).

**Results:** We observed significant associations with PRS for T1D and percentage BMI/weight change from baseline to the endpoint at P-value threshold=0.0022 (R²=0.02, p=0.03), as well as presence/absence of significant weight gain at PT=0.00015 (R²=0.02, p=0.047). In contrast, we observed no significant associations with PRSs for SCZ, BMI, or T2D and AIWG (p>0.05). However, our findings with T1D would not remain significant after correction for multiple testing according to the Bonferroni method.

**Discussion:** To the best of our knowledge, this is the first study examining whether PRSs for various metabolic-related phenotypes are associated with AIWG in patients with SCZ. Our findings suggest a possible role for PRS of diabetes type 1 being associated with risk for AIWG. This observation would indicate that (auto)immune processes might be related to AIWG which has not previously been reported. Further studies with larger sample sizes and individuals of various ethnic ancestries are required.

**M173. RISK OF SCHIZOPHRENIA AMONG INDIVIDUALS OF AFRICAN AND LATINO ANCESTRY: THE GENOMIC PSYCHIATRY COHORT (GPC) ANALYSES**

Abstract not included.

**M174. REDUCED CHEMOKINE SIGNALLING CAPACITY IS ASSOCIATED WITH INHIBITORY INTERNEURON DYSFUNCTION IN SUBCORTICAL BRAIN REGIONS IN SCHIZOPHRENIA AND BIPOLAR DISORDER**

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**Background:** The subependymal zone (SEZ) adjacent to the lateral ventricles represents the largest reservoir of postnatally-generated cortical and striatal inhibitory interneurons in the human brain. Expression of markers representing the generation of neuronal progenitors from neural stem cells is reduced in the adult SEZ in schizophrenia and bipolar disorder; however, underlying mechanisms and relationships to inhibitory interneuron dysfunction remain unknown. Stem cell maintenance, neuronal migration and cell survival are regulated by signaling of the CXC motif chemokine 12 (CXCL12) through CXC motif chemokine receptors 4 (CXCR4) and 7 (CXCR7), which are increasingly implicated in the pathophysiology of psychiatric disorders.

**Methods:** Post-mortem tissue was obtained from 33 schizophrenia, 32 bipolar disorder and 33 control cases from the Stanley Medical Research Institute. SEZ and caudate nucleus tissue was dissected from 60 µm sections for RNA isolation and cDNA synthesis. Gene expression of CXCL12, CXCR4 and CXCR7 were determined by quantitative polymerase chain reactions. Semi-partial correlations were performed to assess whether CXC chemokine family member mRNAs may correlate with