transverse temporal regions surviving correction for multiple testing (d's > 0.15, q<0.05, corrected).

Mean IQ test scores were lower in both FDRs-SZ (d=-0.42, p<0.001) and FDRs-BD (d=-0.23, p=0.045); while relatives did not differ on EA from controls. The IQ-EA correlation was r=0.39 [0.31–0.47]. When adjusting for IQ or EA, the group differences in brain measures changed, albeit modestly. In FDRs-SZ, controlling for IQ explained part of the effect of familial risk for schizophrenia in total brain, gray and white matter volumes (i.e., reduced effect sizes), while in FDRs-BD IQ correction resulted in a larger average ICV compared to controls.

Discussion: This study showed differential patterns of cortical thickness and surface area abnormalities in FDRs-SZ and FDRs-BD. While present in both relative groups, cognitive deficits (but only IQ not EA) were more pronounced in FDRs-SZ. We found no evidence that larger ICV in FDRs-BD was related to IQ, suggesting that the differential brain developmental trajectories underlying predisposition for schizophrenia or bipolar disorder may be unrelated to IQ. These large-scale studies inform the debate on whether schizophrenia and bipolar disorder represent truly independent diagnostic categories or whether they fall on a continuum of overlapping symptom profiles.

M167. MACHINE LEARNING CLASSIFICATION OF FIRST-EPIODE PSYCHOSIS USING CORTICAL THICKNESS IN A LARGE MULTICENTER MRI STUDY

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Background: Machine learning classifications of first-episode psychosis (FEP) using neuroimaging have predominantly analyzed brain volumes. Some studies examined cortical thickness data, but most of them have used parcellation approaches with data from single sites, which limits claims of generalizability. To address these limitations, we conducted a large-scale, multi-site analysis of cortical thickness comparing parcellations and vertex-wise approaches. By leveraging the multi-site nature of the study, we further investigated how different demographic and site-dependent variables affected predictions. Finally, we assessed relationships between the predictions and clinical variables.

Methods: 428 subjects (147 females, mean age 27.14) with FEP and 448 (230 females, mean age 27.06) healthy controls were enrolled in 8 centers by the ClassiFEP group. All subjects underwent a structural MRI (sMRI) session and were clinically assessed. Cortical thickness parcellation (68 areas) and full cortical maps (20484 vertices) were extracted. Supervised (linear Support Vector Machine) classification was used to differentiate FEP from HC, within a repeated nested Cross-Validation (CV) framework through the NeuroMiner software. In both inner and outer CVs, a 10-fold CV cycle was employed. We performed repeated nested CV at the outer cross-validation cycle by randomly permuting the participants within their groups (10 permutations) and repeating the CV cycle for each of these permutations. As feature preprocessing, regression of covariates (age, sex, and site). Principal Component Analysis and Scaling were applied. All preprocessing steps were implemented within the CV. Further analyses were conducted by stratifying the sample for MRI scanner, sex and by performing random resampling with increasingly reduced sample sizes.

Results: Vertex-wise thickness maps outperformed parcellation-based methods with a balanced accuracy (BAC) of 66.2% and an Area Under the Curve of 72%, compared to a BAC of 59% and an Area Under the Curve of 61% obtained with the ROI-based approach. The two BACs were significantly different based on the McNemar’s Test. By stratifying our sample for MRI scanner, we increased the overall BAC to more than 70% and we also increased generalizability across sites. Temporal areas resulted the most influential regions in the classification. The predictive decision scores presented significant correlations with age at onset, duration of treatment and the presence of affective vs non-affective psychosis.

Discussion: Cortical thickness could represent a valid measure to classify FEP subjects, showing temporal areas as potential markers in the early stages of psychosis. The assessment of site-dependent variables allowed us to increase the across-site generalizability of the model, thus attempting to address an important machine learning limitation, especially in the framework of large multi-site cohort and big data analysis.

M168. CLINICAL-ANATOMICAL PHENOTYPES OF SCHIZOPHRENIA

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Background: Although widespread structural brain abnormalities have been consistently reported in schizophrenia, their relation to the heterogeneous clinical manifestations is not well understood. Multivariate methods are needed to uncover covariance patterns between multiple symptom dimensions and system-wide brain imaging data.

Methods: This cross-sectional study used structural magnetic resonance imaging and neuropsychological data from 133 patients with chronic schizophrenia (48 female. 34.8±13.2 years) from the Northwestern University Schizophrenia Data and Software Tool (NUSDAST). We estimate disease-related voxel-wise tissue volume loss using deformation-based morphometry (DBM) of T1 weighted images. In patients with schizophrenia, multiple clinical dimensions including positive/negative symptoms and cognitive deficits, demographic data as well as individual tissue volume loss (DBM) were included in the multivariate model. Clinical-anatomical phenotypes were identified using partial least squares analysis.

Results: Multivariate analysis revealed three distinct clinical-anatomical phenotypes accounting for 27.5%, 15%, and 13% of the shared covariance between clinical-behavioural data and tissue volume loss (total of 55.5%). The first clinical-anatomical phenotype encompassed cognitive impairments, severity of negative symptoms and tissue volume loss within the default mode network and visual network. The second clinical-anatomical phenotype was associated with additional cognitive
imperfections 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 \((a^\times b)\) the effect of socioeconomic status on clinical outcome (cognitive performance and negative symptoms) \((a^\times b= -0.033(0.008); \text{P} < 0.05 \times 10^{-4}; 95\% \text{ CI } [-0.049, -0.018])\). 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 of patients identified and replicated hundreds of Single-Nucleotide Polymorphism (SNPs), each exhibiting only a modest effect. The analysis of genomic Copy Number Variations (CNVs) allowed us to characterize the structural variants conferring significant risk by disrupting multiple genes involved in neurodevelopmental pathways, and linked to SCZ. In this scenario, the aim of our study is to carry out a genetic characterization of a cohort of patients affected by SCZ, in order to assess the risk of recurrence, to elucidate putative pathogenetic mechanisms and, whenever possible, to conceive tailored interventions and therapies.

Methods: 34 patients (8 women and 26 men) affected by SCZ and admitted to Day Hospital at Psychiatric Division for Treatment Resistant Psychosis of the University of Naples Federico II were recruited, and underwent: i) psychopathological evaluation and assessment of clinical response to antipsychotics; ii) genetic counseling; iii) further diagnostic investigation by using Comparative Genomic Hybridization (CGH) + Single Nucleotide Polymorphism (SNP) microarray with 2x400k Agilent's platform “Genetisure” for detecting unbalanced chromosomal abnormalities and regions of homozygosity (ROHs).

Results: Structural pathogenetic rearrangements resulted in 9 (27%) patients. Those identified were the following: 15q13.3 deletion, 16p13.11 duplication, 22q11.22 deletion (TOP3B), 22q11.22 (PRODH, DGR5, DGR6), RBFOX1 deletion, TCF4 deletion, derivative X chromosome (X;Y translocation).

Potentially pathogenic rearrangements, involving genes associated with psychiatric disorders or implicated in neurodevelopment, resulted in 15 patients (44%). No relevant CNVs were detected in 10 patients (29%), although they showed the presence of ROHs that may contain susceptibility loci, since many neurodevelopmental genes map onto or near these specific regions. Certain of these rearrangements occur in many patients, and certain patients showed likewise multiple rearrangements.

Discussion: The analysis of CNVs and SNPs allowed us to characterize the genetic disease structure in the whole cohort of patients and helped to refine the diagnosis in a few cases, thereby ascertaining an underlying specific genetic condition. A further extension of the study, in terms of sample size and more accurate investigations (i.e genetic mapping of ROHs) is underway. According to literature, rare risk-associated CNVs account for 2% of SCZ cases, but their higher prevalence (27%) in our sample may be influenced by a larger percentage of Treatment Resistant and more severely ill patients (since they were recruited in a highly specialized Unit for Treatment Resistant Psychosis). Therefore, our future purpose is to demonstrate a robust genetic modulation of Treatment Resistant endophenotypes of SCZ.

Moreover, we believe that the role of genetic counseling in psychiatric services should be emphasized, and that genetic testing in this field should not be restricted to suspected childhood neuropsychiatric disorders. According to the neurodevelopmental hypothesis of SCZ, that suggests a brain development disruption in early life (due to genetic and early environmental factors), prompting to a subsequent later emergence of the disease in adulthood, even chronic complex adult mental illness, such as SCZ, deserves detailed investigations and a more exhaustive genetic evaluation.

M171. THE GENE-SHARING RELATIONSHIP OF SCHIZOPHRENIA WITH OTHER MENTAL OR SYSTEMIC DISORDERS: A DISEASE-SIMILARITY NETWORK ANALYSIS FOCUSED ON EGOCENTRIC NETWORK

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Background: Schizophrenia is an archetypal example that a psychiatric illness may not merely be a mental or a brain disorder but rather a systemic illness. It can be glimpsed from a wide range of biomarkers that span all the imaginable body systems, and from higher co-morbidity with other systemic illnesses. Therefore, quantitative analysis of schizophrenia’s relationship with 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 automated 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