S184. Machine Learning Reveals Deviance In Neuroanatomical Maturity Predictive Of Future Psychosis In Youth At Clinical High Risk

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Journal Title: Schizophrenia Bulletin
Volume: Volume 44, Number suppl_1
Publisher: Oxford University Press (OUP): Policy B - Oxford Open Option D | 2018-04-01, Pages S396-S397
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1093/schbul/sby018.971
Permanent URL: https://pid.emory.edu/ark:/25593/tdxf7

Final published version: http://dx.doi.org/10.1093/schbul/sby018.971

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Accessed April 16, 2019 5:08 AM EDT
S182. CHANGE IN CORTICAL MORPHOMETRY IN INDIVIDUALS WITH PERSISTING PSYCHOTIC EXPERIENCES: A LONGITUDINAL PILOT STUDY
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Background: There is an increasing interest in the presence of psychotic symptoms in the general population that do not meet the threshold for psychotic disorder. Such psychotic experiences (PEs) are more prevalent than conditions such as schizophrenia and often manifest during childhood and adolescence. PEs are a risk factor for psychotic disorders and a range of adverse psychosocial outcomes. PEs can become abnormally persistent with a corresponding increase in psychiatric morbidity. Previous research has highlighted subtle deviations in brain structure associated with the presence and persistence of PEs, but longitudinal assessments are needed to gauge if these deviations continue, perhaps as part of an atypical neurodevelopmental trajectory.

Methods: Longitudinal imaging data, taken at ages 20 and 25, were available for 25 young adults who were part of an MRI nested case control study within the Avon Longitudinal Study of Parents and Children. They were selected originally on the basis of presence or absence of PEs. Cortical surface data were analysed using FreeSurfer. Presence of PEs was assessed at ages 18, 20, and 25 and we defined persistence as endorsing PEs at multiple time-points. Average cortical volume and thickness were extracted from each brain parcellation. We additionally calculated fractal dimensionality (FD) of each parcellation using a box-count algorithm to capture shape complexity. We compared the rate of change between healthy controls (HC) and those with persistent PEs in each parcellation and used permutation testing to control for multiple comparisons.

Results: Both HC and PEs showed the expected age-related net loss in brain volume; an increase in white matter volume offset by a greater reduction in grey matter. We identified greater volume loss in PEs in the left parietal lobe and further examination of local volume highlighted additional changes. PEs were associated with a greater rate of volume loss in the anterior cingulate, postcentral, and lingual gyrus in the left hemisphere and in the right inferior parietal lobule and pars orbitalis. Thinning of the left inferior parietal lobule was greater in those with PEs. There was further converging evidence of focal abnormalities in the left postcentral gyrus in terms of reductions in cortical thickness and FD in PEs. Similarly, we found reduced FD relative to HC in the left rostral anterior cingulate. There was additional evidence for reductions in FD in the left hemisphere in the cuneus, isthmus cingulate, and middle frontal gyrus.

Discussion: Our findings highlight a deviation from typical age-related changes in brain volume in individuals with persisting manifestations of PEs. Though these changes could reflect an acceleration of the typical volume loss that is seen with aging, there are several points of evidence against this. We found no differences in global volume changes and only the left parietal lobule was found to show a greater volume loss in PEs. On a local scale, findings seemed to mostly converge on parietal and cingulate regions in the left hemisphere with some evidence of aberrations in frontal regions. These pilot data are, uniquely, unconfounded by illness and treatment related factors and highlight the continued need for longitudinal assessments of brain structure in relation to PEs; there is an increasing risk of transitioning to a psychotic disorder with persistence of PEs and our findings may reflect the neuroanatomical basis for an anomalous developmental trajectory related to psychotic disorders.

S183. ABNORMALITIES OF FRONTO-SUBCORTICAL PATHWAYS IN SCHIZOPHRENIA AND THE DIFFERENTIAL IMPACTS OF ANTIPSYCHOTIC TREATMENT: A DTI-BASED TRACTOGRAPHY STUDY
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Background: The fronto-striato-thalamic circuitry is a key network associated with several symptoms observed in patients with schizophrenia (SZPs). In this study, we use diffusion tensor imaging (DTI) to investigate the integrity of white matter (WM) pathways involved in this network in SZPs relative to healthy controls (HCs). We also evaluate the differential impact of chronic exposure to clozapine as well as other atypical and typical antipsychotics on fascicular integrity in this network in schizophrenia.

Methods: 63 HCs and 41 SZPs were included in this study. Of the SZPs, 16 were treated with clozapine (SZPsC), 17 with atypical antipsychotics (SZPsA), and 8 with typical antipsychotics (SZPsT). We reconstructed three tracts belonging to the fronto-striato-thalamic network in the left hemisphere using tractography: one fronto-subcortical tract (FSC), one prefronto-subcortical tract (PFSC), and one prefronto-frontal tract (PFF). Diffusion parameters were individually extracted in each tract.

Results: SZPs exhibited lower integrity in both the FSC and PFSC relative to HCs, and SZPsT patients showed altered integrity compared to SZPsC patients. There were no WM integrity differences in the PFF between SZP groups or between SZPs and HCs.

Discussion: These results suggest that SZPs exhibit structural connectivity abnormalities in the prefronto-fronto-subcortical network that are specifically and differentially impacted by the type of antipsychotic treatment. Additional studies are needed to separate the contributions of clozapine-mediated neuroprotection, neurotoxicity related to typical antipsychotics, and the illness itself to the observed differences.

S184. MACHINE LEARNING REVEALS DEVIANCE IN NEUROANATOMICAL MATURITY PREDICTIVE OF FUTURE PSYCHOSIS IN YOUTH AT CLINICAL HIGH RISK
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1Yale University; 2University of Calgary; 3University of California, Los Angeles; 4University of California, San Diego; 5The Zucker Hillside Hospital; 6University of California, San Francisco; 7University of North Carolina; 8Harvard Medical School; 9Emory University; 10University of California, Irvine

Background: Both early (pre- and perinatal) and late (adolescent) neurodevelopmental disturbances are hypothesized to contribute to the pathophysiology of schizophrenia. Disturbances originating earlier in life (e.g., resulting from the interplay of genetic factors and obstetric complications) would be expected to affect brain integrity from birth onwards and could therefore help to explain cases with subtle deficits in premorbid functioning during childhood and earlier ages at onset of full psychosis (i.e., early to mid-teens). In contrast, disturbances that emerge during late adolescence and early adulthood (e.g., via abnormal neuromaturational events and/or environmental factors) could help to explain cases with normal premorbid features.
S185. DTNBP1 IS ASSOCIATED WITH THE AGE AT ONSET OF KOREAN PATIENTS WITH SCHIZOPHRENIA

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Background: The dysbindin gene (DTNBP1) is located in chromosome 6p22.3, one of the regions of positive linkage for schizophrenia. In particular, dysbindin protein has been found to play a role in the glutamate neural transmission in the brain. A strong genetic association between DTNBP1 and schizophrenia has been replicated through many recent studies. However, we have not replicated positive association between DTNBP1 and schizophrenia in our Korean sample. Because schizophrenia has been regarded as a disease with a quite heterogeneous origin and evolution, it is useful to categorize patients with schizophrenia into relatively homogeneous subsets based on clinical characteristics including age at onset (AAO). We investigated the association between DTNBP1 and AAO of schizophrenia.

Methods: We assessed age at first occurrence of positive psychotic symptoms of 197 patients with schizophrenia with DSM IV diagnosis, which was re-evaluated by Korean version of Diagnostic Interview for Genetic Study. Five SNPs, SNPA, P1763, P1320, P1635 and P1655 of DTNBP1 were genotyped and genetic association analyses were performed using the PLINK program.

Results: In SNPA, patients with AT (N=10) showed significant earlier AAO than those with AA (N=187) (p<0.0001). The patients with heterozygote for SNP P1763 (TG, N=40) or P1320 (CT, N=41) also showed significant earlier AAO than those with homozygote (p<0.0001, P<0.0001, respectively). In addition, haplotype of all SNPs (SNPA-P1320-P1635-P1655-P1763) analysis showed significant association with AAO (p=0.000953).

Discussion: In conclusion, although we were unable to support an association between DTNBP1 and schizophrenia, DTNBP1 might play a role in disease modifying. However, considering the several limitations of this study, further research involving different polymorphisms in DTNBP1 and various clinical subsets with sufficient numbers will be required to evaluate the contribution of DTNBP1 to schizophrenia.

S186. KCNH2 POLYMORPHISM ASSOCIATED TO ALTERED EEG FUNCTIONAL NETWORK MODULATION IN SCHIZOPHRENIA

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Background: The rs3800779 polymorphism at KCNH2 gene, which encodes for a Voltage-Gated Potassium Channel Subunit, has been associated with the risk for schizophrenia (SZ) and with changes in the expression of a brain isoform with specific electrophysiological characteristics (Huffaker et al., 2009). It has been hypothesized that the KCNH2 gene variability could be involved in SZ by means of modulating the neuronal excitability. Graph-theory parameters applied to electroencephalographic (EEG) activity are useful to assess functional connectivity in the brain and have shown altered patterns of global connectivity in schizophrenia. We aimed to investigate whether KCNH2 contributes to functional connectivity alterations replicated in SZ patients.

Methods: EEG data were acquired during the performance of an odd-ball task in 50 schizophrenia patients and 101 matched healthy controls. The rs3800779 at KCNH2 was genotyped. From the EEG activity, the Small World (SW) analysis was performed for 50 schizophrenia patients and 101 matched healthy controls. The rs3800779 polymorphism at KCNH2 gene was associated with a Voltage-Gated Potassium Channel Subunit, has been associated with the risk for schizophrenia (SZ) and with changes in the expression of a brain isoform with specific electrophysiological characteristics (Huffaker et al., 2009). It has been hypothesized that the KCNH2 gene variability could be involved in SZ by means of modulating the neuronal excitability. Graph-theory parameters applied to electroencephalographic (EEG) activity are useful to assess functional connectivity in the brain and have shown altered patterns of global connectivity in schizophrenia. We aimed to investigate whether KCNH2 contributes to functional connectivity alterations replicated in SZ patients.

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