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Background: The complex sulco-gyral pattern results from fetal and early childhood processes that shape the cortex anatomy from a smooth lissencephalic structure to a highly convoluted surface. Abnormal brain maturation has been suggested as risk factor for schizophrenia. Thus, measures of the cortical folding pattern could provide cues for the neurodevelopmental aspects of pathopsychology.

Method: Brain morphometry softwares providing 3D sulci descriptors (e.g. surface) from MRI (Mangin, 2004 ; Cachia, 2007). This automatized method avoids biases inherent to image normalisation and partial volume effect. Therefore, statistics on sulcal measurements should generalize across patients. T1 MRI datasets were studied in at-risk subjects, adolescent onset schizophrenia, and patients with treatment-resistant depression and auditory hallucinations.

Results: Decreased in sulci surface were detected in whole brain sulcal indices and in regional sulcal indices. Decreases in global sulcal indices were detected in most patient groups, except in at risk subjects. Decreases in local sulcal indices were detected in langage-related areas in resistant hallucinators (Cachia 2007), and confined to left temporal regions in adolescent schizophrenia (Pentilla, submitted). In patients with treatment-resistant depression, sulci descriptors differed in right hemisphere sulci adjacent to limbic regions (Pentilla, submitted).

Conclusion: The potential of the gyrification pattern for the inference of neuroimage-based developmental biomarkers will be further examined using multivariate classification approaches (Duchesnay 2006).

Reference

[1]. Mangin et al., Neuroimage 2004 - Cachia et al., Neuroimage 2007 – Duchesnay et al., Neuroimage 2006

S39.02

Imaging genetics in the Edinburgh high risk study

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Background: We have recently completed a ten year longitudinal study of brain structure and function in a group of individuals at high risk of schizophrenia for familial reasons, and have taken blood for genetic analyses. We can therefore study the effects of recently discovered candidate genes for schizophrenia in a large well characterised cohort of those at risk, including some who went on to become ill, but without illness related potential confounders such as antipsychotic medication.

Methods: 162 initially healthy people aged 15-25 at high genetic risk of schizophrenia, because they had at least one close relative with the disorder, were recruited and examined with structural MRI and functional MRI. The development of psychotic symptoms and/or schizophrenia itself was monitored at serial assessments, which most participants had at 18-24 month intervals over up to 10 years.

Results: 21 developed schizophrenia during the study and an additional 66 subjects had psychotic symptoms at one or more assessments. 78 of the subjects were genotyped. Single nucleotide polymorphisms in the Brain Derived Neurotrophic Factor (BNDF) and D-amino acid oxidase (DAO) genes were associated with abnormalities of frontal and temporal function in the high risk cohort as a whole. A risk allele (SNP8NRG243177) in the Neuregulin 1 (NRG1) promoter region, on the other hand, was associated with psychotic symptoms, decreased premorbid IQ and decreased activation of pre-frontal and temporal lobe regions. The Val(158)Met polymorphism in the Catechol-O-MethylTransferase (COMT) gene predicted schizophrenia in this cohort in a dose-dependent manner. It was also associated with reduced gray matter density and BOLD signal in anterior cingulate cortex.

Conclusions: These patterns of altered brain structure and function have previously been associated with schizophrenia in this and other samples. In the Scottish population, BDNF and DAO may have trait effects, while the NRG1 variant appears to be a risk factor for an extended or intermediate phenotype and the COMT Val allele is associated with an increased risk of schizophrenia. This genetic background may provide a mechanistic framework in which to study the effects of environmental risk factors, perhaps particularly in subjects at increased familial risk.

S39.03

Candidate genes and brain cortical morphology in schizophrenia

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Aim: To investigate associations between schizophrenia candidate gene polymorphisms and regional cortical thickness and volume in patients with schizophrenia and healthy control subjects.

Methods: Genotyping was performed using PCR and pyrosequencing techniques. Cortical morphology was analyzed by processing magnetic resonance brain images with the FreeSurfer software package. General linear model analysis was used to study associations between gene variants and cortical thickness in patients and controls, respectively. Regional cortical volumes were defined from automatic cortical parcellations. Our first studies from 96 patients with schizophrenia and 104 healthy control subjects demonstrate that polymorphisms in the brain derived neurotrophic factor (BDNF) gene may be associated with variation in frontal lobe morphology. Associations seem to be stronger in patients with schizophrenia than in healthy controls.

Symposium: Psychotherapy of chronic depression – different approaches, equal efficacy?

S45.01

Interpersonal psychotherapy - New results in chronic depression

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