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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).

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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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Interpersonal Psychotherapy (IPT) proved to be effective for the treatment of acute depressive episodes for which it was originally developed. However, for chronic depression (dysthymia), IPT with or without pharmacotherapy did not show a benefit over pharmacotherapy alone in terms of symptom reduction (Browne et al., 2002; Markowitz et al., 2005). In the study of Markowitz et al. (2005) it was not even superior to the control condition. However, the investigations using IPT with dysthymic patients had some shortcomings such as the use of a non-modified version of IPT (Browne et al., 2002) or insufficient statistical power (De Mello et al., 2001; Markowitz et al., 2005).

Data reanalysis from a larger study (Schramm et al., 2007) with 45 inpatients suffering from chronic Major Depressive Disorder that were randomized to 5 weeks of either combined treatment with IPT (15 individual and 8 group sessions) plus pharmacotherapy or to standard treatment (pharmacotherapy plus Clinical Management). The study included a prospective naturalistic follow-up, 3- and 12-months after discharge.

The brief, but intensive combined treatment program had significant acute and long-term benefits over medication monotherapy in chronically depressed inpatients. In summary, while limited by some factors, the results of this study provide hope that with intensive treatment chronically depressed patients have a good chance of getting well relatively quickly and with lasting effects.

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S45.02

Cognitive behavioral therapy of chronic depression

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There are a few studies available about cognitive behavioural treatment of mild chronic depressive disorders (dysthymia). These studies adapted only classical elements of shortterm cbt to this special group of patients. There are only clinical impressions and some case reports for cbt with more severely chronic depressed cases. I plan to present some general ideas about chronic depression and implications for cbt intervention. Our model of an intensive form of outpatient psychotherapy with chronic major depression has ten moduls over 45 to 60 individual sessions. We only have first experiences on single case level. More sophisticated and controlled studies are planned but will not start before we have more data to evaluate effect sizes and decide about appropriate outcome measures. The presentation will lay out the few available results of published studies, describe out treatment rationale and elements (moduls), and hopes to stimulate interest in more engagement to work and to investigate chronic depression.

S45.03

Cognitive Behavioral Analysis System of Psychotherapy (CBASP) - A new approach for chronic depression

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Background: Chronic depressions are difficult to treat. A new form of psychotherapy, CBASP, has been specifically developed for this subgroup of depressed patients by James McCullough (USA). In a large multisite randomized controlled trial, the combination of CBASP with antidepressant medication was considerably more effective than antidepressants alone (response rates of 73% versus 48% respectively). Therefore, CBASP is regarded as an evidence based therapy for chronic depression and mentioned in most depression treatment guidelines. Yet, the dissemination of this form of psychotherapy is still limited.

Methods: In the Netherlands, 25 therapists were trained by McCullough, and participate in a recently started (June 2007) randomized controlled trial, comparing CBASP with usual care in outpatient psychiatric clinics. The basic structure of the CBASP sessions is cognitive behaviorally oriented. Patients are learned to perform analyses of specific situations, and bring in and discuss a situational analysis form every session. As this approach alone often fails in chronic depressed patients, who are often emotionally detached and avoidant, other techniques are used to develop a - therapeutic relationship, and to confront the patient with his/her behavior and opportunities to change. These techniques concern transference issues, and so-called disciplined personal involvement of the therapist.

Results: This presentation will focus on the content of the CBASP therapy and on our experiences in learning and providing CBASP. Additionally, the study design of the randomized controlled trial will be presented.

Conclusion: CBASP is an interesting and promising treatment for chronically depressed patients.

Interactive Clinical Session: Visions in the treatment of schizophrenia

YP08.01

Catie and Star*D

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After great anticipation and with high expectations the initial results of the CATIE (Schizophrenia) and the Star*D (Depression) studies have been published. Many results have been inconclusive, but more importantly, most significant outcomes have been highly controversial - from the inclusion criteria, patients selection, outcome measures used for evaluating efficacy, to the lack of full randomization and the doses used.

This presentation will present a review of both studies' results, covering the data that have been published thus far, and address some of the controversies.

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