

## Symposium: Altered white matter communication in schizophrenia and bipolar disorder: A possible common endophenotype?

### S32.01

Uncinate fasciculus and cingulum bundle findings in first episode schizophrenia and first episode bipolar disorder: A diffusion tensor imaging study

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**Background and Aims:** Fronto-temporal connections have long been thought to be involved in schizophrenia. Two fronto-temporal connections of interest are uncinate fasciculus (UF) and cingulum bundle (CB), which recently have been investigated using Diffusion Tensor Imaging (DTI), a new technique that affords an opportunity to evaluate white matter fiber integrity in vivo. Using this technique, we previously reported abnormalities in UF and CB in chronic patients. Additionally, we noted that schizotypal personality disordered subjects showed UF but not CB abnormalities.

**Methods:** Here, we sought to determine whether or not UF and CB white matter integrity are altered at initial onset of illness, and are specific to schizophrenia. We evaluated twelve first-episode schizophrenia, 12 first-episode affective psychosis and 12 controls using DTI on a 1.5T magnet. Fractional anisotropy (FA) and mean diffusivity (Dm) were used to quantify water diffusion, and cross-sectional area was defined with a directional threshold method.

**Results:** Findings showed bilateral reduction of UF FA, but not Dm, in first-episode schizophrenia compared with controls and first-episode affective psychotic patients. For CB, there were no statistically significant group differences for either FA or Dm.

**Discussion:** These findings suggested that UF white matter integrity, but not CB white matter integrity, is altered at initial onset of schizophrenia and may be specific to schizophrenia. In contrast, CB abnormalities are not present at first episode of schizophrenia and may reflect progressive changes that occur over the course of the illness. The latter will need to be investigated using a longitudinal design.

### S32.02

White matter volume in the schizophrenia and bipolar spectrum

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Structural brain imaging abnormalities in schizophrenia-resemble spectrum disorders in many respects. Similar to schizophrenia, cerebrospinal fluid (CSF) is increased and cortical volumes are decreased in schizotypal personality disorder (SPD). In this large sample study,

MRI assessed white matter volumes and diffusion tensor anisotropy was assessed in the schizophrenia spectrum. The sample includes 230 schizophrenics (ages 13-78) and an approximately age matched group of 81 patients with schizotypal disorder and 230 normal volunteers. For the bipolar spectrum there were 44 patients with bipolar spectrum disorder. Results in a pilot subsample of patients revealed increases in white matter in the cingulate in SPD and Schizophrenia in comparison to the normal sample. However in prefrontal regions, a schizophrenia spectrum pattern was observed with greater white matter increases in patients with schizophrenia than patients with schizotypal disorder, and greater gray matter decreases in patients with schizophrenia than patients with schizotypal disorder. Anisotropy changes were widely observed across the prefrontal cortex and corpus callosum. Taken together these results suggest that prefrontal change appears associated with a continuous spectrum deficit while some changes in the cingulate and other brain regions may show protective or reactive change in schizotypal patients. Bipolar patients had significantly reduced volume of the white and the gray matter of the frontal cortex. Furthermore, compared with control subjects, BPS patients as a group showed alterations in anisotropy of the internal capsule adjacent to the striatum and thalamus and the frontal white matter.

### S32.03

Evidence of shared white matter disruption in bipolar disorder and schizophrenia

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There is strong qualitative and quantitative evidence of white matter abnormalities in schizophrenia and bipolar disorder from structural magnetic resonance imaging (MRI). There is also good evidence of altered connectivity in schizophrenia using diffusion tensor magnetic resonance imaging, but no study has yet addressed the diagnostic specificity of these findings or whether they are related to specific susceptibility genes.

**Methods:** Diffusion tensor MRI was used to assess white matter integrity in patients with bipolar I disorder (BD) (n=42), schizophrenia (n=28) and healthy controls (n=38). Clinically stable patients with one other close family member with the same diagnosis were selected. In a second study, we examined white matter associations with Neuregulin I in a sample of healthy controls. Fractional anisotropy (FA) was compared between the groups using voxel-based morphometry, automated region of interest analysis and probabilistic tractography. Results : Patients with BD and those with schizophrenia showed reduced FA in the anterior limb of the internal capsule, anterior thalamic radiation and uncinate fasciculus compared with controls. Results from the second study showed reductions in those carrying a Neuregulin I variant previously associated with psychotic symptoms.

**Conclusions:** Reduced white matter density and integrity is common to both schizophrenia and BD. It is likely that this shared white matter disruption is determined in part by shared genetic risk factors.

### S32.04

Cytoarchitecture alterations of white matter in schizophrenia and bipolar disorder

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Kraepelinian dichotomy between schizophrenia (SCZ) and bipolar disorder (BD) is based on the increased degree of overlap in the pathophysiology of the two disorders and white matter pathology has emerged as a possible marker for these illnesses. Indeed, genes regulating myelin and oligodendrocytes are downregulated in both SCZ and BD, suggesting oligodendrocyte dysfunction. Also, we and others have demonstrated using MRI intra- and inter-cortical white matter impaired connectivity in both disorders. These accumulating data suggests a possible common physiological pathway for SCZ and BD, involving white matter disconnection. White matter microstructure organization can now be explored by diffusion imaging. Recently, we have shown with diffusion MRI impairment of frontal and temporal white matter, corpus callosum, and thalamus in one of the largest population of patients with SCZ reported in the literature. Also, white matter microstructure alterations have also been found in BD, and our diffusion imaging data would confirm that in our population of BD patients. Therefore there is strong evidence suggesting that white matter pathology is present in both SCZ and BD, possibly representing a common intermediate endophenotype. This may potentially be sustained by dysfunctional oligodendrocytes, leading to white matter disruption and ultimately to cognitive disturbances. Impairments of executive functions are indeed reported in both SCZ and BPD and epidemiological studies have demonstrated family aggregation of both disorders. In conclusion, in this symposium we hope to inform on the current debate on the merits of the Kraepelinian dichotomy, characterizing the dimensional approach in the understanding of the functional psychoses.

useful. Administrative staff rated outcome measures as more valuable than did clinical staff.

**Conclusions:** The results have implications for the implementation and sustainability of routine outcome measurement. It is helpful to distinguish between clinicians' views as to the general value of outcome measurement, which is often positive, and their experience of ease of use, which may be much less positive. The results highlight the need for staff to receive targeted training and usable reports, and to have access to resources to extract value from outcome measures.

## S20.02

Effect of outcome monitoring and management in German inpatient psychiatric care: Cluster-randomised trial

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**Background and Aims:** Outcome management has been suggested as a promising strategy to improve quality of mental health care. However, there is a lack of evidence on the efficacy of feedback of treatment outcome to people with severe mental disorder and their clinicians. Thus, the study "Outcome monitoring and outcome management in inpatient psychiatric care" (EMM) aims to ascertain the short- and mid-term effect of outcome management in inpatient psychiatric care.

**Method:** This cluster-randomised trial started in June 2005. 294 participants who gave informed consent have been recruited among patients admitted to a large psychiatric hospital in rural Bavaria. These were asked to provide information on treatment outcome on the Outcome Questionnaire 45 via weekly computerised assessments. Patients and clinicians in the intervention group received continuous feedback of outcome.

**Results:** Patients were willing and able to provide outcome data on a regular basis. Patients highly valued feedback of outcome while clinician acceptance was moderate. At discharge, there were no differences between the feedback and no-feedback groups on patient-rated outcome. However, as compared to the no-feedback group, length of stay of patients with good outcome who received feedback was shorter while it was longer for those with unfavorable outcome. Further findings on the mid-term effect of feedback at follow-up and on the cost-effectiveness of the intervention will be reported.

**Conclusions:** Implications of these results for further improving the effectiveness of outcome management in mental health services and thus contributing to an adaptive allocation of treatment resources will be discussed.

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## Symposium: Mental health outcome assessment and feedback: An international perspective

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### S20.01

Attitudes of clinicians to routine outcome measurement in mental health

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**Background and Aims:** Routine outcome measurement is mandated in public mental health services in Australia, but uptake and compliance is variable. This may be because of uncertainties and resistances among clinicians. The objective of this study was to survey attitudes and experiences to routine outcome measurement among staff in adult area mental health services and to understand their correlates.

**Methods:** As part of a larger study, a specifically designed questionnaire was distributed to all staff.

**Results:** The questionnaire return rate was high. A wide range of opinion was found, ranging from very positive to very negative, with the majority being somewhat positive. Staff who had attended training reported the measures as easier to use than those who had not. Staff who had recently seen feedback of their outcome measures rated outcome measures as more valuable but less easy to use than those who had not seen feedback. Compared to other disciplines, medical staff and psychologists tended to rate outcome measures as less

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## Symposium: Clinical development of antipsychotic drugs

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### S37.01

Interpretation of data for the regulatory agency, for the scientific community and for practicing psychiatrists

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