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# Symposia

## S1. Functional imaging of psychotic symptoms

*Chairs*: R Murray (UK), M Spitzer (D)

### S1-1
PATHOPHYSIOLOGY OF THOUGHT DISORDER IN SCHIZOPHRENIA

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Factor analyses of clinical ratings suggest that thought disorder is heterogenous, with 'positive' and 'negative' components. The former is characterised by speech which appears disorganised, while the latter corresponds to speech which is impoverished in content or quantity. This study examined the patterns of neural activity associated with expression of 'positive' and 'negative' thought disorder. PET was used to measure regional cerebral blood flow (rCBF) while 6 dextral male patients with schizophrenia were describing ambiguous pictures. This procedure elicits thought disordered speech, with the severity varying from picture to picture. Subjects were scanned 12 times, with a different picture presented before each scan. The severity of 'positive' and 'negative' thought disorder during each scan were assessed using the Thought, Language & Communication Index, then correlated with rCBF across the 12 scans within each subject, using statistical parametric mapping. The analysis controlled for the number of words articulated per scan, eliminating effects due to variation in the amount of speech produced. 'Positive' thought disorder was correlated with activity in the parahippocampal region and inversely correlated with activity in the inferior frontal, cingulate and left superior temporal cortex ($p < 0.001$). 'Negative' thought disorder (corresponding mainly to poverty of content) was inversely correlated with activity in dorsolateral prefrontal cortex and the left superior temporal cortex ($p < 0.003$). These observations are consistent with the notion that thought disorder is heterogenous, but also suggest that both its 'positive' and 'negative' components are associated with defective function in areas responsible for the generation and monitoring of language.

### S1-2
MEG-BASED EVIDENCE OF ACCELERATED AUDITORY PROCESSING IN SCHIZOPHRENIA

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Prior event-related potential (ERP) studies in schizophrenics have demonstrated diminished inhibition to the second P50 response using two-stimulus paradigm. Besides ERP, cerebral processing can also be studied with magnetoencephalography (MEG). Previous MEG-studies have demonstrated that P50m and N100m auditory responses appear somewhat earlier over the contralateral than over the ipsilateral auditory cortex to the ear stimulated in healthy subjects. We investigated with a 122-channel whole-head magnetoencephalography, which enable one to measure simultaneously brain activity in both hemispheres, whether early parallel auditory processing is impaired in schizophrenia. Sequences of tone pips were monaurally presented to 11 schizophrenic patients and to 21 healthy controls in a passive condition. The event-related magnetic fields (ERFs) were recorded simultaneously over both auditory cortices. The interhemispheric latency difference of the P50m, but not that of the N100m, was significantly shorter in the patient group in the right-ear but not in the left-ear stimulus condition. Furthermore, the ipsilateral P50m was significantly earlier in schizophrenics in the right-ear condition. This suggest that schizophrenics have accelerated ipsilateral auditory processing in the right hemisphere possible due to altered inhibition.

### S1-3
IS CORTICAL RESPONSIVITY INCREASED IN SCHIZOPHRENICS PREDISPOSED TO HALLUCINATIONS?

P.W.R. Woodruff[1,2]*, N. Blackwood[2], Y. Ha[2], I.C. Wright[2], E.T. Bullmore[2], M. Brammer[2], R.J. Howard[2], S.C.R. Williams[2], J. Shapleske[2], S. Rossell[2], R.M. Murray[2]. [1]*Manchester University and Salford Mental Health Trust;* [2]*Institute of Psychiatry, London, UK*

We explored the hypothesis that schizophrenics with a history of auditory hallucinations (trait positive, T+), would show greater responsivity of temporal cortex to the modulatory effects of auditory selective attention than schizophrenics without a history of AH (trait negative, T–).

Functional magnetic resonance imaging (FMRI) was used to measure blood oxygenation level dependent signal induced by auditory selective attention in right-handed male subjects: i) 8 T+ schizophrenics (none of whom were currently hallucinating); ii) 7 T– schizophrenics, and iii) 8 healthy volunteers. We performed voxel-by-voxel comparisons of the median power of response to selectively attending to auditorily presented numbers versus passive listening, and passive listening versus background noise.

Schizophrenic patients exhibited a greater temporal cortical response than healthy controls when listening passively to numbers.

Responsivity to attentional modulation in temporo-frontal language regions was greater in T+ than T– patients, and showed a different distribution pattern.

These results suggest that the predisposition to auditory hallucinations may denote altered sensitivity of the temporal cortex to the modulating influence of attention to auditory stimuli.

## S1-4
No abstract received

## S1-5
WHAT CAN FUNCTIONAL IMAGING TELL US ABOUT THE AETIOLOGY OF SCHIZOPHRENIA?

R.M. Murray*, E. Bullmore. *Institute of Psychiatry, de Crespigny Park, London SE5 8AF, UK*

Functional brain imaging is generally concerned with pathophysiology rather than aetiology. Recent studies suggest that schizophrenic patients are characterised by i) abnormal functional connectivity between language areas; and ii) reversal of the normal asymmetry (left greater than right) in temporal lobe activation in response to external speech. How might such abnormal physiology arise? When brain lesions occur in adult life, then one may expect deficits in function. However, the brain which has been compromised early in development may have sufficient plasticity to enable it to develop compensatory neurocognitive networks; dysfunction rather than simple loss of function may subsequently arise.

Auditory hallucinations appear to result from dysfunctional connectivity between fronto-temporal language systems. Furthermore, decrease in the normal correlations in volume between frontal and temporal structures in schizophrenia, implies that the dysfunctional connectivity arises out of dysplastic brain development. That the language dysfunction is developmental in origin is supported by cohort studies demonstrating that preschizophrenic children show an excess of difficulties in the acquisition of speech.

Cohort studies also report that preschizophrenic children have an excess of mixed and uncertain hand and eye dominance. Indeed, there is much evidence of abnormal laterality and symmetry in schizophrenia. Since normal cerebral asymmetry develops in the latter part of foetal life, this also appears developmental in origin. Studies of families multiply affected with schizophrenia show that both the ill individuals and those non-psychotic individuals (obligate carriers) who appear to be transmitting the liability to the disorder show this loss of normal asymmetry, indicating that it has a genetic basis; it is not yet clear whether the obligate carriers show similar functional abnormalities to schizophrenics. In addition, obstetric complications are found in excess in schizophrenia, and appear to be responsible for the abnormal asymmetry of hippocampal volume often found in schizophrenia; obstetric complications, particularly preterm birth are also known to be associated with later development of hand dominance.

# S2. Assessment of disablement

*Chairs*: B Üstün (CH, WHO), C Pull (LUX)

## S2-1
DISABLEMENT AND MENTAL ILLNESS

Charles Pull. *Centre Hospitalier de Luxembourg, Luxembourg*

Several studies in the last couple of decades have demonstrated that diagnosis of mental disorders alone does not predict outcomes, treatment response, and resource utilization. This has led to a shift in focus from diagnosis to disablement to understand the consequences of health conditions. The dimension of disablement has been the subject of recent study and has especially highlighted the role of mental disorders in the overall global burden of disease. Studies will be reviewed in the context of the ongoing revision of the International Classification of Impairments, Disabilities and Handicaps of the World Health Organization as the framework for understanding disablement related to mental disorders.

## S2-2
THE DEVELOPMENT OF THE WHO-DAS II

Somnath Chatterji. *World Health Organization, Geneva, Switzerland*

The assessment of disablements has been fraught with several problems related to terminology, conceptual framework, methods of elicitation, grading of responses and item difficulty and psychometric reliability and validity. In view of this, the WHO-NIH Joint project on assessment and classification of disablements related to Alcohol, Drug use and Mental (ADM) disorders reviewed over 300 instruments and sought expert consultation to develop an assessment of disablement (WHO DAS II) that would meet these criticisms and be cross culturally applicable. The development process of the schedule will be described.

## S2-3
THE FIELD TRIALS OF THE WHO-DAS II

Juergen Rehm. *University of Hamburg, Hamburg, Germany*

The WHO-DAS II is designed to meet rigorous criteria of reliability, validity and sensitivity to change. It is intended to be cross culturally applicable and provide a common metric across physical and mental disorders. The instrument has been pre-piloted in five countries and is under extensive testing in 18 countries at present. The methodology for the field trials will be described and initial results will be presented.

## S2-4
RESULTS OF THE WHO-DAS II TESTS IN THE UK

Nicholas Glozier. *Institute of Psychiatry, London, UK*

The WHO-DAS II was field tested in London in a community psychiatry sample of 100 subjects for feasibility, applicability and acceptability. Trained interviewers interviewed subjects and a cognitive debriefing exercise was carried out to elicit feedback on the interview. The initial results will be described and the suggestions for change will be discussed.

## S2-5
THE EU INITIATIVE ON ASSESSMENT OF DISABLEMENT RELATED TO MENTAL DISORDERS

Venos Mavreas. *Eginition Hospital, Athens, Greece*

The WHO-DAS II is being tested along with the ICIDH-2 in 6 countries in Europe: the UK, Spain, Greece, Italy, Luxembourg and Netherlands as part of a EU initiative. Respondents have been selected from the major categories of neuro-psychiatric disorders according to the ICD-10 criteria. Initial results from the different sites and client groups will be presented. Comparisons with the larger WHO international field testing will be discussed.