

into individual practices was carried out for the full year of the study. Group B (control group) will be educated in the second year.

The range of outcome variables being assessed include general practitioner's identification index, patient's outcome for depression, prescription of antidepressants, referrals to secondary care, suicide rates, and the cost effectiveness of the intervention. Methodological and practical issues will be presented.

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## S27. The brain imaging of psychopathology

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### SIMILARITIES AND DIFFERENCES BETWEEN SCHIZOPHRENIA AND AFFECTIVE DISORDERS

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Functional brain imaging techniques can be broadly divided into two categories: "brain mapping" procedures which measure regional cerebral blood flow or metabolism as an index of neural activity and radioligand studies which may be used to obtain measures of enzyme / receptor activity, density or affinity and possibly fluxes in endogenous neurotransmitters. To date only brain mapping techniques have been used extensively in the study of the neurophysiological correlates of psychopathology. Brain mapping studies in psychiatric patients have most commonly been used with a cross-sectional design to identify changes in the pattern of brain activity in patient groups in comparison with an appropriate control group. Patients have been scanned in an "activated" state while performing a task designed to highlight specific aspects of their psychopathology, or at "rest", in which case persistent symptomatology (such as depressed mood or hallucinations) is considered the activating state. In other studies the neurophysiological variable (e.g. regional cerebral blood flow) is correlated with a relevant measure of psychopathology within the patient group. These techniques have been used extensively in schizophrenia and to a lesser degree in patients with affective disorders. They have established with increasing reproducibility that distributed abnormalities of brain function occur in the major psychiatric disorders, with some relationship to symptom or syndrome profiles. Indeed there is some evidence that the overlap in results from cross-sectional studies in schizophrenia, depression and other affective disorders is due to the presence of common symptoms across diagnosis. The longitudinal comparison of patients before and after recovery is a conceptually simple but underused method of examining the relationship between cerebral dysfunction and psychopathology. Such studies have shown that lateral prefrontal cortical function in depression normalises with clinical recovery. The challenge for functional imaging is now to further probe these identified dysfunctions with more refined methods that have greater sensitivity and which may ultimately be able to define the relationship between a particular pattern of abnormal brain function, specific psychopathology and a biochemical mechanism. The progress that has been made in this endeavour and future strategies will be presented with particular reference to "brain mapping" activation studies in schizophrenia and depression and developments in radioligand studies.

### FUNCTIONAL BRAIN IMAGING OF NEGATIVE SYMPTOMS OF SCHIZOPHRENIA

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Negative schizophrenic symptoms are poorly responsive to neuroleptic medication, and may be heterogeneous, since it is difficult to discriminate primary, enduring negative symptoms from those secondary to long-term neuroleptic treatment, depression, or institutionalisation. It has been hypothesized that they may be related to a deficient dopaminergic transmission, to a functional hypofrontality, or to structural abnormalities.

First, we studied negative symptoms and dopaminergic variables. In order to investigate the links between dopamine D2 (postsynaptic) receptors and primary negative symptoms, young, drug-free negative schizophrenics were selected. The measure of the striatal D2 receptors assessed by positron tomography (PET) correlated negatively to the score of a dimension of psychomotor poverty, involving the core negative symptoms alogia and blunting of affects [1].

At the presynaptic level, the dopaminergic function was studied with PET and 18F-FluoroDOPA, using the Patlak method in 6 non-neuroleptized schizophrenics and controls. The variance of the 18F-Dopa uptake constant Ki was significantly increased in patients: the 18F-Dopa uptake constant Ki was markedly increased in some, but not all, schizophrenics, and decreased in catatonia.

Second, the links between the negative symptoms and the cerebral regional activation abilities are currently studied using the H<sub>2</sub><sup>15</sup>O method, measuring the regional cerebral blood flow changes through lexical evocation tasks. In negative patients, preliminary results suggest a hypofrontality in the resting state, and preservation of the capacity to activate some frontal regions during the tasks, although with a somehow different pattern of regional activation than in controls.

[1] Br J Psychiatry 1994 164, 27-34.

### FUNCTIONAL NEUROANATOMY OF VERBAL SELF-MONITORING

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*Background:* Cognitive psychological models and functional neuroimaging data suggest that auditory verbal hallucinations may result from the disordered monitoring of inner speech. However, the brain regions involved in normal verbal monitoring are unknown. We sought to identify them by examining the neural response to alterations in auditory verbal feedback during reading aloud, so that the speech that was perceived sounded different to the speech that was articulated.

*Methods:* Regional cerebral blood flow was measured with positron emission tomography and H<sub>2</sub><sup>15</sup>O while 6 dextral male controls articulated single words, presented at 2s intervals on a VDU. Each subject had 12 scans. The baseline task involved reading aloud and hearing one's own speech. Verbal monitoring was engaged in two conditions. In the first, the pitch of the subject's speech was elevated by 8 semitones with an acoustic effects unit. In the second, their speech was substituted with that of an investigator, who articulated the words in synchrony with the subject. The tasks were matched for volume of auditory input, and were presented in a counterbalanced order. Data were analysed with Statistical Parametric Mapping.