

## New Research

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### **NRI. Schizophrenia: neuroimaging**

*Chairmen:* M Revelly, P Grasby

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#### **NORMAL PLANUM TEMPORALE ASYMMETRY IN FAMILIAL SCHIZOPHRENIA: A VOLUMETRIC MRI STUDY**

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Loss or reversal of the normal asymmetry of the planum temporale has been reported in schizophrenia. Brain asymmetries are established in utero and are thought to be under genetic control. Abnormalities in brain lateralization are therefore assumed to be indicative of genetic vulnerability to schizophrenia. We tested this hypothesis in a sample of schizophrenics from multiply affected families where genetic factors appear to operate predominantly. We compared 31 (20 men and 11 women) right-handed schizophrenics to 35 (18 men and 17 women) right-handed matched community controls. Volumetric measures of the planum temporale were obtained from 3D reconstructed MRI images. Volumes were calculated using the Cavalieri method. Asymmetry coefficients obtained from the patients did not differ significantly from those obtained from the controls. Sex specific analysis did not reveal any differences either. Our study suggests that abnormalities in the planum temporale asymmetry may not be present in familial schizophrenia.

#### **A MONOZYGOTIC SCHIZOPHRENIC TRIPLET**

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A male monozygotic triplet, now 36 years old, is described. At age 20, within 8 months the three men independently developed acute schizophrenic disorders (DSM-III-R) with auditory hallucinations, bizarre delusions, and thought disturbances. There were similarities between the triplets with regard to the chronic intermittent course of the disorder, the decline of social adjustment and loss of working capacity. The psychoses responded promptly to conventional neuroleptic treatment. Neuropsychological assessment demonstrated similar marked reductions of attentional, mnemonic and executive functions. MRI showed similar borderline ventricular enlargements and widened subarachnoidal spaces over frontoparietal and basal regions as well as around the pituitary gland (empty sella). All the men had a right sided hearing defect with a reduction of the ossicular bones. Cytogenetic investigations demonstrated an extra band at chromosome 15p. The parents of the patients appeared to be mentally healthy, they reported no hearing difficulties. The father, but not the mother, exhibited the chromosomal 15p aberration. The

father demonstrated widened subarachnoidal spaces frontally and in basal regions similar to those of the triplet. The mother had an empty sella. Other possible clues to etiological mechanisms for the psychotic disorders was a possible influenza infection in the mother during the first trimester. It appears most likely that DNA aberrations may be responsible for the great similarities in the psychoses, the reductions of neuropsychological functions, the morphological MRI changes, the right sided ossicular reductions.

#### **NEUROIMAGING FINDINGS IN PATIENTS WITH POSTPARTUM PSYCHOSES**

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CT abnormalities have been observed in a variety of psychoses. Although most literature concerns schizophrenic psychoses, findings are not specific. Further elaborating upon a set of CT scans of young and middle-aged women with a history of postpartum psychosis the ventricular and cisternal CSF spaces were quantified in 14 patients. 12 of whom had cycloid psychoses with postpartum onset according to Leonhard (1979) and Perris & Brockington (1981). When compared to age-matched patients with cycloid psychoses or bipolar affective disorders outside the puerperium left ventricular area, planimetric VBR, and cisterna supravermis volume were significantly larger in the postpartum psychosis group. This finding may reflect an additional vulnerability marker in psychoses of the puerperium.

#### **SIMPLE SCHIZOPHRENIA REVISITED: A CLINICAL, NEUROPSYCHOLOGICAL AND BRAIN IMAGING ANALYSIS**

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The concept of simple schizophrenia, first described by Diem in 1903 and accepted by both Kraepelin and Bleuler, has since become a controversial entity. DSM-IV does not include a categorisation for simple schizophrenia, and ICD-10 recommends caution in diagnosing it. The contemporary literature on the disorder is very small [1,2].

We have collected 8 patients who meet provisional diagnostic criteria for simple schizophrenia [2]. As well as undergoing detailed clinical review, all were also administered a comprehensive neuropsychological battery. Structural neuroimaging (CT plus MRI in selected cases) and functional neuroimaging (SPECT) were also carried out.

Clinically, these patients conformed to the classically described picture of simple schizophrenia. Despite long histories in most cases, there was no evidence of any more than fleeting and equivocal positive symptoms. Neuropsychologically, all the patients displayed a pattern of impairment similar to that observed in cases of chronic schizophrenia, with IQ decline, memory impairment and impairment of executive ('frontal') function, coupled with preservation of lan-

guage and visuo-perceptual function. Structural neuroimaging was typically normal, but SPECT scanning revealed a high frequency of abnormalities; in all cases these affected temporal and frontal regions and sometimes they were marked enough to raise the possibility of organic brain disease (which was, however, never substantiated).

- [1] Stone, AA et al. *Am J Psychiatry*, 1968, 125, 305–312.  
 [2] Black, DW, Boffeli, TJ. *Am J Psychiatry*, 1989, 146, 1267–1273.

### QUANTITATIVE EEG IN MEDICATED AND UNMEDICATED SCHIZOPHRENICS: EVIDENCE FOR HYPER-STABILIZED BRAIN FUNCTION

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The scalp EEGs of 32 medicated chronic schizophrenic patients, 12 unmedicated chronic schizophrenics and 35 matched healthy controls were analyzed by adaptive segmentation. This is an automated procedure which determines the sequence and duration of topographical defined brain electric fields in continuous EEG. EEG segments, during which one characteristic field prevails are thought to represent "microstates" of brain functioning. Data were acquired during a rest condition, a mental arithmetic task, and a CNV paradigm. Results indicate prolonged duration of brain microstates in both unmedicated and medicated schizophrenics. Topographic variability, when compared across the different tasks, was also significantly reduced in both schizophrenics groups. Increased microstate duration remained a constant feature of the schizophrenics EEGs, independent of the task. From task to task, schizophrenics as well as normal controls showed consistent changes of electric field topography and of EEG microstate duration. However, the topography of the microstates during the tasks was significantly different in both schizophrenic groups from that of controls. Neuroleptic medication correlated negatively with microstate duration in a dose-dependent way. There was an inverse relationship between topographic variability and negative symptoms as well as BPRS scores. It is concluded that the temporal-spatial characteristics of brain electric activity indicate a reduced array of functional modes and enhanced stability of brain electrical microstates in schizophrenia.

### REGIONAL CEREBRAL ACTIVATION DURING WORD PRODUCTION IN NEGATIVE SCHIZOPHRENIA

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In schizophrenics, frontal activation deficits have been observed during cognitive paradigms requiring the patients to generate responses restricted by the task instructions, thus diminishing spontaneous "free-wheeling" thought associations. In order to investigate the capacity of schizophrenic patients to increase their regional cerebral blood flow during controlled, and more spontaneous mental states, we used two word production tasks. The first one was the verbal fluency, which activates left hemisphere and particularly frontal regions in right-handed controls, and is generally impaired in negative schizophrenics. The second one was the continuous free word association, allowing more spontaneous changes in the course of word associations.

**Subjects and Methods:** Normalized regional cerebral blood flow (NrcBF) was measured using a positron tomograph with H<sub>2</sub><sup>15</sup>O.

Ten DSM-III-R schizophrenics with marked negative symptoms, and twelve controls (all subjects were right-handed men with similar age and verbal level), were compared in 2 runs of 3 conditions: rest, verbal fluency, and continuous free word association. NrcBF and individual 3D magnetic resonance images (MRI) were aligned, allowing definition of volumes of interest having anatomical boundaries. NrcBF were compared using MANOVA with a two level Group factor (patients and controls) and a three level within-group Task factor.

**Results:** In patients, lower NrcBF values were found at rest and in both tasks, in right frontal regions (Brodmann's areas 8 and 6), right anterior cingulate, whereas higher NrcBF values were present in both striata.

In both groups, a NrcBF increase in most left prefrontal regions was detected during both word production tasks.

During both word production tasks, the NrcBF increase was greater in controls in regions involved in verbalization: left primary motor, right cerebellum. These differences will be compared to the subjects' performances. A NrcBF decrease in the right supra marginalis gyrus of controls was not observed in schizophrenics. During continuous free word association, the pars opercularis of the right frontal gyrus and the adjacent part of the right middle frontal gyrus were activated in patients but not in controls.

**Conclusion:** The pattern of regional activation in negative schizophrenics differs partially from that of controls, involving a higher magnitude of activation in circumscribed right frontal regions homologous to Broca's area during spontaneous word production, and no deactivation of the right supra marginal gyrus in both word production tasks. However the capacity to activate left dorsolateral prefrontal regions persists in negative schizophrenia. Thus, in this disorder, there is no general activation defect across all cognitive tasks challenging the prefrontal regions. Lastly, striata perfusion appears abnormally increased at rest and during word production tasks.

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## NR2. Neuroimaging and neuropsychiatry

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### LIMBIC SYSTEM DYSFUNCTIONS IN MANIA AND SCHIZOPHRENIA USING <sup>18</sup>F-FLUORODEOXYGLUCOSE AND POSITRON EMISSION TOMOGRAPHY

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Positron emission tomography (PET) with <sup>18</sup>F-labelled fluorodeoxyglucose (FDG) was used to examine the regional cerebral metabolism of glucose in the limbic regions in 15 patients with mania (Catego Class M\*) and 17 patients with schizophrenia (14, Catego Class S\* & 3, Catego Class P\* and. Also, 6 patients with psychotic depression (Catego Class D+), 4 with non-psychotic depression (Catego Class R\*) and 10 healthy volunteers were imaged for comparison. Subjects were all right handed and were imaged at rest with the eyes closed and ears unplugged.

Four sections at 63 mm, 76 mm, 83 and 89 mm from the brain vertex, based on the atlas of Aquilonius and Eckernäs (1980), were imaged. FDG region specific uptake relative to the uptake in all