guage and visuoperceptual 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).

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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 temporospatial 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 $H_2{}^{15}O$. Ten DSMIIIR 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.

NR2. Neuroimaging and neuropsychiatry

Chairmen: P McGuire, M Ron

LIMBIC SYSTEM DYSFUNCTIONS IN MANIA AND SCHIZOPHRENIA USING ^{18}F-FLUORODEOXYGLUCOSE AND POSITRON EMISSION TOMOGRAPHY

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Positron emission tomography (PET) with ^{18}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

regions of interest (ROI's) was determined for 28 ROI's (14 left & 14 right) including the amygdala, hippocampus, parahippocampal gyrus, mediofrontal cortex (including anterior cingulate), caudate, lentiform nucleus, thalamus and prefrontal, temporal and occipital neocortex.

A significantly increased relative uptake of FDG in the right amygdala was found in all "psychotic" patients compared to the normal controls. In the schizophrenic patients, the significant increase above normal controls was limited to the right amygdala and right parahippocampal gyrus, whereas in the affective disorder groups (both psychotic and non-psychotic) there were widespread increases across other limbic structures. Significant decreases in relative FDG uptake were apparent only in the left mediofrontal cortex in the schizophrenic and manic groups in comparison to the normal controls.

These results might be accounted for by an increase in dopaminergic input into limbic areas, which is generalised to most limbic regions in the affective disorders and localised to the right amygdala and right parahippocampal regions in schizophrenia.

ANGER AND SADNESS: A PET STUDY OF AFFECTIVE MEMORY

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Introduction. Adverse life events can induce enduring mood states and precipitate overt psychiatric disorder. We have investigated the neurophysiological mechanism whereby the recollection of life events associated with anger and sadness rekindles the emotional experience.

Methods. Male volunteers were studied with $H_2{}^{15}O$ Positron Emission Tomography, images were analysed by Statistical Parametric Mapping.

Results. Recollection of neutral memories was associated with activation of the cortex of the medial temporal pole predominantly on the right. Recollection of events associated with anger activated the insula, anterior cingulate, inferior frontal and premotor cortex and the caudate nucleus. Recollection of sad events also activated the insula and caudate nucleus. Comparison of the anger and sadness conditions revealed activation of the ventro-medial striatum specifically associated with sadness and of the anterior cingulate and inferior frontal cortex associated with anger.

Conclusions. Pathways from the medial temporal cortex to the striatum and insula constitute a neurophysiological substrate for the association of affect and memory. Affective disorder may reflect a pathophysiological interaction between psychological and constitutional factors in this network.

A SELECTIVE INTERHEMISPHERIC TRANSFER CALLOSAL DEFICIT IN AUTISM

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Here we examined autistic children for lateralised and interhemispheric transfer abnormalities. Two studies were carried out, ten years apart, on groups of English and Welsh children. In the first children matched textures by touch. In the autistic group (N = 24) there was a selective impairment in contralateral matching between the hands but not in ipsilateral matching. The interhemispheric deficit was not found in four control groups consisting of mentally disabled children of either the same mental or chronological age as the autistics and normal children matched on the same criteria. In the second experiment 20 autistic children were compared with 20 mentally handicapped children of the same mental and chronological ages. The task involved matching geometric shapes by active touch, which is more clearly lateralised than the passive touch task above. Again no lateralised deficit was disclosed and in replication of the first study the autistic group was impaired in contralateral matching in both left to right and right to left directions. The results are discussed in the light of contemporary theories of neurodevelopmental anomalies in autism, here implicating the corpus callosum.

D2 DOPAMINE RECEPTOR BINDING BEFORE AND AFTER TREATMENT OF MAJOR DEPRESSION MEASURED BY SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

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Previous *in vivo* studies demonstrated changes in regional cerebral blood flow and glucose metabolism as well as alterations of the opioid system within the frontal cortex in depression. The present study continues the search for specific biochemical alterations in depression and investigates the potential impact of serotonin reuptake inhibition on the dopaminergic system. As yet, 11 patients (age 53.0 ± 10.8 ys., mean ± SD, 8 f, 3 m) with major depression were investigated before and immediately following a six week treatment with the selective serotonin reuptake inhibitor (SSRI) paroxetine (40 mg/d) or fluoxetine (up to 60 mg/d). Dopamine receptor binding was estimated using the specific D2/D3 receptor antagonist 123I-iodobenzamid (IBZM, 185 Mbq) and SPECT (double head camera PRISM 2000, Picker Ohio) with high resolution collimation. Specific IBZM binding was calculated as the region of interest to cerebellum ratio.

The total score in the Hamilton Depression Rating Scale (HAMD) decreased from mean ± S.D. 27.6 ± 4.9 before treatment to 13.5 ± 9.1 after treatment.

Within the basal ganglia, the average IBZM binding remained unchanged in the group as a whole. However, there was a significant correlation between the change of striatal IBZM binding and the improvement in psychopathology ($p < 0.05$), i.e., responders demonstrated a 20% increase and nonresponders a 10–20% decrease or no change of striatal and cingulate IBZM binding.

These preliminary data of an ongoing prospective study suggest an increase of dopamine D2/D3 receptors during successful therapy of major depression with an SSRI, which is consistent with findings of dopamine D2/D3 receptor sensitization in animal studies.

RETROGRADE AMNESIA IN PATIENTS WITH TEMPORAL LOBE, FRONTAL LOBE AND DIENCEPHALIC LESIONS

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The aim of this study was to investigate retrograde amnesia in patients who had either temporal lobe, diencephalic or frontal lobe lesions. The groups contained patients with herpes encephalitis, Korsakoff syndrome and recent frontal tractotomy. Patients were assessed for background variables such as severity of anterograde amnesia, current IQ and performance on executive/frontal lobe tasks.

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