We present preliminary data on the IRR based on 10 sessions, see table.

The findings seem promising with respect to the achievement of an even better IRR which will result from increasing raters experience.

CATEGORICAL AND DIMENSIONAL ASSESSMENT OF PERSONALITY DISORDERS: AN INTEGRATIVE APPROACH

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Categorical and dimensional models of personality, personality disorders (PD) and their interrelation will be discussed under the hypothetical perspectives, that higher order personality factors structure the personality of normal persons as well as of the mentally ill, and that no fundamental, but only a gradual difference exists between normal personalities and PDs. The relationship between this categorical conceptualization of the PDs and the dimensional factor model of personality was examined by using the Aachen Inventory for the Assessment of Personality Disorders (AIPD) that provides a typological assessment of 11 abnormal personalities covering all criteria of DSM-III-R and ICD-10, and the self report scale "Sechs Faktoren Test" (SFT) to measure higher order factors of personality as neuroticism, aggressiveness, conscientiousness, openness to experience, extraversion and religious attitude. The following relations were expected: 1) Personality disorders can be suitably assigned to superordinated clusters of personality factors. 2) Personality disorders can be appropriately explained in terms of the "big five" personality disorders. 3) "Neuroticism" will be a common factor closely related to all personality disorders.

Data have been collected from a sample of 168 psychiatric inpatients consecutively admitted to hospital care and included irrespective of their clinical diagnosis, and a general population sample (N = 100). Cluster Analysis was used as a categorial approach and Similarity Structure Analysis (SSA) as a dimensional method. Using SSA, an empirical structure of the interrelations among the different personality disorders and the personality factors can be presented allowing interpretations based on Guttman's Facet Theory. The question of continuity is also analyzed at the opposite pole, i.e. the relationship between axis I mental disorders and axis II personality disorders.

IMPULSIVE BEHAVIOUR AND GENES IMPLICATED IN SEROTONIN NEUROTRANSMISSION: AN ASSOCIATION STUDY

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A preliminary but growing body of evidence supports the existence of genetic and biological substrates of impulsive behaviour. In particular, there is an extensive literature suggesting that impulsive behaviour in animals as well as in humans may be influenced by a dysfunction of the central serotonergic system, Genes coding for enzymes, transporters or receptors playing a key role in serotonin neurotransmission are likely to be involved in impulse control regulation. We hypothesize that genotypes of these key proteins could be different in individuals exhibiting impulsive behaviours. We report preliminary results of an ongoing association study on genotypes of tryptophan hydroxylase, monoamine oxydase A, monoamine oxydase B, serotonin receptor 1a and serotonin receptor 2c. In this study, inpatients are screened for the presence of impulsive behavioural tendencies using a questionnaire adapted from Silverman et al. (1991). Subjects with such tendencies are then assessed with the IPDE and 100 subjects meeting at least one criterion for impulsive personality disorder according to ICD-10 are compared to 100 non impulsive, control subjects. In addition, all subjects will be assessed with the CIDI and those meeting criteria for organic mental disorder, psychotic disorder, a current episode of mood disorder, or mental retardation are excluded. Controls are subjects without any impulsive behavioural tendencies nor personal history of psychiatric illness, including personality disorder.

S83. 20 years of functional neuroimaging: cerebral blood flow/metabolism

Chairmen: L Pilowsky, A Lishman

STUDYING THE EFFECTS OF DOPAMINE NEUROTRANSMISSION WITH FUNCTIONAL IMAGING

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An abnormality in dopaminergic neurotransmission has been the cornerstone of theories as to the causation of schizophrenia. How do the findings of regional dysfunction and disturbances in cortical integration relate to proposed dopamine disturbances? One mechanism is via the modulatory effects of dopamine on regional, and inter regional, brain function. Novel applications of functional imaging techniques can be used to provide links between modulatory neurotransmitters and psychological function using combined pharmacological and neurocognitive challenges. Experiments in which manipulation of dopaminergic neurotransmission and cognitive activation are combined will be described. These show that it is possible to link neurotransmission to neuropsychological functioning and, more importantly, specify the neuroanatomical sites of interaction.

These experiments provide the background to a study of schizophrenic patients in which we examined the effect of a dopaminergic manipulation, with apomorphine, on the neural response to a cognitive task. In the schizophrenic patients, relative to controls, an impaired cognitive activation of the anterior cingulate cortex was significantly modulated by a manipulation of dopaminergic neurotransmission. Following apomorphine the schizophrenic subjects, relative to the controls, displayed a significantly enhanced activation of the anterior cingulate cortex. Furthermore, abnormal patterns of interaction between prefrontal and temporal cortices in the non drug condition were modulated by dopamine perturbation.

[1] Dolan RJ, Fletcher P, Frith CD, Friston KJ, Frackowiak RSJ and Grasby PM (1995) Dopaminergic modulation of impaired cognitive activation in the anterior cingulate cortex in schizophrenia. Nature, 378, 180–182.

THE FUTURE OF FUNCTIONAL IMAGING IN PSYCHIATRY

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Until recently most functional imaging in psychiatry centered around positron emission tomography (PET) and single photon emission tomography (SPET); deriving measures of either cerebral blood flow (as an index of neural activation) or central receptor populations (as in dopamine D_2 receptor number). The development of non-invasive

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functional MRI questions the utility of PET/SPET measures of cerebral blood flow to index neural activation. However, PET and SPET have an assured future mapping distributed neurochemical and neurotransmitter systems *in vivo*. Although radiotracer development has essentially concentrated on imaging central receptors, increasing effort is being applied to study 'dynamic' aspects of neurotransmission such as endogenous neurotransmitter release *in vivo*. In addition, the relationship between central receptor occupancy and clinical/therapeutic effects remains relatively unexplored for many psychotropic medications. The measurement of neurotransmitter synthesis rates and second messenger systems, where technically feasible, will be of considerable importance. Furthermore PET and SPET radiotracers may increasingly provide a neurochemical account of the reported regional abnormalities of neural activation associated with psychiatric syndromes and symptoms.

MAGNETIC RESONANCE SPECTROSCOPY (MRS) AS A TOOL TO STUDY THE NEUROPATHOLOGY OF SCHIZOPHRENIA

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We have used MRS to study in vivo biochemical parameters indicative of the neuropathological abnormalities present in schizophrenia. 25 right-handed patients fulfilling RDC criteria for schizophrenia and 32 aged-matched controls were included in the study. Using a GE Signa 1.5 T Scanner, MRS was performed in volumes of interest of between 4–9 cm^3 in both hippocampi. NAA, choline and creatine were quantified. Schizophrenics showed a significant loss of NAA in the left hippocampus compared to controls, less severe losses were detected on the right. These were not correlated with age or duration of illness and probably represent a static neuronal loss.

In addition, in schizophrenics there was an age-related choline loss not found in controls. This abnormality may be due to a progressive abnormality of myelination which could explain the clinical deterioration observed in some patients and the progressive structural abnormalities described in some follow-up imaging studies.

No correlations were observed between MRS parameters and cognitive abnormalities present in schizophrenics.

MRS is an important tool to study the neuropathology of schizophrenia in vivo and to gain information about its natural history.

S84. Driving performance of psychiatric patients, before and during anxiolytic and antidepressant therapy

Chairman: JF O'Hanlon

RISK OF TRAFFIC ACCIDENT INJURY AFTER BENZODIAZEPINE USE

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The objective of this presentation will be to assess the risk of injuries due to traffic accidents after a first prescription for a benzodiazepine (BZD). Saskatchewan Health supplied study populations of 78,000 adults who received BZD hypnotics (triazolam and flurazepam), 148,000 who received BZD anxiolytics (lorazepam, diazepam, and oxazepam) and 98,000 unexposed controls. These populations were monitored for subsequent hospitalizations for traffic accident injury. Persons taking BZD hypnotics showed an odds ration (OR) of 3.9 (1.9–8.3), while those taking BZD anxiolytics showed an OR of 2.5 (1.2–5.2) for hospitalization due to traffic accidents within four weeks of filling the prescription for BZD. Within two weeks of prescription, the OR rises to 6.5 (1.9–22.4) for hypnotics and 5.6 (1.7–18.4) for anxiolytics. Within the first week, the OR are even higher at 9.1 and 13.5, respectively. Each of the five individual BZD showed a similar pattern, with oxazepam showing the lowest curve. The highest age/sex risk groups were young males. Concomitant use of antidepressants, antipsychotics, or anticonvulsants showed no statistically significant additional risk for injury. From a public health view, the high OR for traffic accident injury after BZD use are of concern, and action for prevention is advisable.

ROLE OF BENZODIAZEPINE COMEDICATION IN DETERMINING DEPRESSED PATIENTS DRIVING PERFORMANCE DURING ANTIDEPRESSANT (FLUOXETINE AND MOCLOBEMIDE) THERAPY: RESULTS OF A POST HOC ANALYSIS

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Outpatients suffering from Major Depression (DSM IIIR; HAM-D scores > 17) were tested for driving ability twice on separate days in a standardized on-the-road test and then randomly assigned to two groups for double-blind treatment with fluoxetine 20 mg gd (N = 19) and moclobemide 150 mg b.i.d. (N = 21) lasting 6 weeks. Clinical assessments were repeated after 1, 2, 3 and 6 weeks using HAM-D, MADRS and CGI. Doses were doubled after 3 weeks for patients who failed to improve. Driving assessments were repeated after 1, 3 and 6 weeks. The test involved operating an instrumented vehicle over a 100 km primary highway circuit while attempting to maintain a constant speed (95 km/h) and steady lateral position between boundaries of the slower traffic lane. The primary outcome variable was standard deviation of lateral position (SDLP), an index of road tracking error or allowed "weaving". There were no significant differences in mean improvements on clinical rating scales or side-effect frequencies between groups. Patients' driving performances were normal and reliable ($r = 0.87$) during tests before treatment. Most patients' driving performances changed little but some in both groups showed a progressive deterioration. A post hoc multiple regression analysis was applied to identify the responsible factor(s). Among hypotheses tested was that the benzodiazepine (BZD) comedication, which was permitted under the protocol for 31 patients who had been chronic users, interacted with the antidepressants to impair performance. This was confirmed by a significant ($p < 0.03$) relationship. Patients whose driving deteriorated used BZDs that are metabolized by a cytochrome P450 isozyme subject to inhibition by their particular antidepressant. Those using other BZDs, or none, drove consistently well. Moreover, this relationship was independent of the BZD doses (d.d.d. units). The implication for future confirmation is that neither fluoxetine nor moclobemide impair driving performance, except when used with metabolically incompatible BZD comedication.

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