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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