

acteristics of the conventional neuroleptics, in particular, at doses considerably lower than previously examined.

It has been proposed that the "atypical" properties of clozapine is explained by its simultaneous interaction with 5-HT<sub>2</sub> and D<sub>2</sub> receptors. We have demonstrated very high (85–90%) 5-HT<sub>2</sub> receptor occupancy and low (20–67%) D<sub>2</sub> receptor occupancy in patients treated with low to moderate doses of clozapine. This finding supports the position of the 5-HT<sub>2</sub> receptor as potential mediator of atypical effects. The putative atypical antipsychotics risperidone and olanzapine induced high occupancy of both D<sub>2</sub>- and 5-HT<sub>2</sub> receptors at clinically relevant doses. Further clinical characterization of such new compounds will thus provide valuable leads to the clarification of atypical antipsychotic action.

#### IN VIVO RECEPTOR SPET STUDIES OF ANTIPSYCHOTIC DRUG ACTION

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Nuclear medicine techniques (positron emission (PET)- and single photon emission tomography (SPET)) now permit examination of brain receptors in living subjects. As these receptors are targeted by antipsychotic drugs, hypotheses concerning drug action may now be tested in vivo. In particular, schizophrenic nonresponders and responders to classic antipsychotic drugs show similar levels of D<sub>2</sub> blockade by the drugs. The atypical antipsychotic drug clozapine has beneficial effects without high striatal D<sub>2</sub> receptor blockade. We will report data showing the novel atypical drug, olanzapine occupies striatal D<sub>2</sub> receptors to the same low extent as clozapine. However, another new atypical antipsychotic drug, sertindole, like risperidone, shows high levels of striatal D<sub>2</sub> blockade but few extrapyramidal side effects. These data will be discussed in the light of recent theories as to the neuropharmacology of schizophrenia.

## S78. New perspectives in psychiatric epidemiology

Chairmen: H Hafner, J Angst

#### EPIDEMIOLOGY OF SEXUAL PROBLEMS AND DYSFUNCTIONS IN THE COMMUNITY

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Representative community studies of sexual dysfunctions are almost non-existent. Two studies have been conducted on middle aged women [1,2], but no studies of males have been launched as yet.

In the Zurich cohort study 591 males and females were interviewed five times during a 15 year period, from ages 20–35. At age 35, 69% of the subjects were still in the study. Sexual dysfunctions were assessed in one section of a broad semi-structured interview carried out by clinical psychologists. The prevalence rates obtained were cumulatively gathered over the five interviews and weighted back to the normal population.

Emotional sexual problems were found in 21% (males 12.6, females 29.2), low sexual desire in 29% (males 23%, females 35.1%) and functional problems in 17% of cases (males 10.5%, females

23.3%). Sexual dysfunctions were found to be associated with depression, anxiety disorders and insomnia, but no association with other functional somatic syndromes was recorded. Females differed from controls in their elevated scores of neuroticism and autonomous lability as found by Osborne et al. [2]. Moreover, females were characterised by low self-esteem and mastery and by increased avoidance coping strategies. Subjects with children developed sexual problems more frequently and these were usually caused by difficulties in partnerships and core family.

- [1] Garde K, Lunde I: (1980) Social background and social status: influence on female sexual behaviour. A random sample of 40 year old Danish women. *Maturitas* 2: 241–246.
- [2] Osborn M, Hawton K, Gath D: (1988) Sexual dysfunction among middle aged women in the community. *BMJ* 296: 959–962.

#### CEREBRAL VENTRICLE DIMENSIONS AS RISK FACTORS FOR SCHIZOPHRENIA AND AFFECTIVE PSYCHOSIS: AN EPIDEMIOLOGICAL APPROACH TO ANALYSIS

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The literature on neuroimaging in psychosis contains many references to, so called, "enlargement" of some structures, the dimensions of which vary continuously throughout the population with considerable overlap between affected and unaffected groups. Is this concept of enlargement valid?

A case-control study was undertaken of volumetric computerized tomographic scan measures in 216 consecutive admissions for functional psychosis and 67 healthy community controls. Odds ratio analysis demonstrated significant linear trends in the association between increasing lateral and third ventricle volumes, and both RDC schizophrenia ( $N = 121$ ) and schizo-affective disorder ( $N = 41$ ); cases were consistently associated with larger volumes than controls. There was an association between larger third, but not lateral, ventricle size in affective psychoses ( $N = 54$ ). These associations were statistically independent of intracranial volume, sex, social class and ethnicity, factors which were significantly associated with ventricular measures in the controls and presumably, in the general population. There was no evidence of a threshold corresponding to the notion of normal versus enlarged ventricles.

#### GENETIC EPIDEMIOLOGY OF FUNCTIONAL PSYCHOSES

W. Maier.

The presentation will focus on schizophrenia and bipolar affective disorder.

During the last decades a broad variety of studies explored the patterns and the determinants of the familial aggregation of the major psychiatric disorders. As most other common diseases all functional psychoses are aggregating in families.

The diagnostic specificity of the familial patterns of aggregation is low. Particularly with affective disorders occurring more frequently than expected by chance in families of probands with schizophrenia. The various subtypes of both disorders are not breeding true in families with the single exception of bipolar affective/schizo-affective disorders.

Family, twin and adoption studies clearly demonstrated that both disorders are of multifactorial origin. Although the specific nature of causes is widely unknown it is evident that genetic as well as environmental factors (familial as well as individual) are contributing as it has also been shown for other common diseases.

A variety of specific putative environmental factors for the multiple occurrence of psychiatric disorders in families have been explored. However, methodological limitations prohibit conclusive results on the specific nature of the predisposing environmental risk factors.

The available tools for the identification of causal and/or susceptibility genes are more stringent. Previous claims of predisposing genes for both disorders did not pass the test of replication. Very recently, multiple susceptibility genes for schizophrenia as well as for bipolar disorder were found in a replicable fashion. Current evidence emerging from genetic association and linkage studies in schizophrenia and bipolar disorder will be reviewed.

#### NEW PERSPECTIVES ON THE CLINICAL EPIDEMIOLOGY OF SCHIZOPHRENIA

**B. Nowotny, H. Häfner.** *Central Institute of Mental Health, PO Box 12 21 20, D-68072 Mannheim, Germany*

In this paper clinical epidemiology is used as an approach to explain the onset, development and course of schizophrenia. The period before first admission becomes especially important because the analysis of onset and development of symptomatology allows for the following:

1. To discriminate precipitating events from social consequences of the illness and to compare the social biography of the future patients with the biography of an age and sex matched control group from the general population. The ABC schizophrenia study, an investigation of the early course of a large epidemiologically defined first episode sample, has shown that already in the prodromal phase the illness causes age and sex specific effects on success in fulfilling social roles.

2. Cognitive deficits prior to onset of the illness or developmental disorders in childhood have been observed and have supported the hypothesis, that schizophrenia is in part caused by an early developmental disorder of the brain.

3. The gender difference in age at onset, tested on different investigational levels in the ABC study, and the second peak in rates of women around menopause have been explained by means of the oestrogen hypothesis of schizophrenia on the epidemiological level. This hypothesis has also been supported in animal studies, neurochemical analyses and controlled clinical studies.

A further hypothesis of sub-types of schizophrenia is for example a narrowly defined S+ schizophrenia based on neurodevelopmental disorders occurring mostly among young men and a benign form of the disorder usually a spectrum diagnosis occurring mostly in women usually several years older than their counterparts. The effort to determine empirical sub-types based on symptomatology in the early course, illness behaviour, further course and other factors within the ABC schizophrenia study yielded not very stable sub-types without any differences in gender distribution.

We can conclude, that symptomatology and the course, of schizophrenia are partly determined by age at onset, gender and developmental factors.

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## S79. Substitute prescribing and substance dependence

*Chairmen:* M Farrell, B Ritson

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#### BUPRENORPHINE IN THE TREATMENT OF OPIATE ADDICTION. EUROPEAN STATUS

**Marc Auriacombe.** *Université de Bordeaux II, Faculté de Médecine Victor Pachon, Centre Carreire, 121 rue de la Béchade, 33076 Bordeaux, France*

This presentation will review the clinical and pharmacological basis for the rational use of buprenorphine for the treatment of opioid dependence. The first clinical report on the use of buprenorphine will be presented as well as a comprehensive review of the clinical data currently available from treatment centre based treatment settings. Long-term outcome results of buprenorphine treatment from office-based practice setting will be discussed, and the specifics of buprenorphine treatment in France will be presented as well as results from ongoing evaluation research.

#### DELIVERY OF METHADONE MAINTENANCE IN THE EUROPEAN UNION

**Michael Farrell, Jan Neeleman, Michael Gossop, Paul Griffiths, Emily Finch, John Strang.** *National Addiction Centre, 4 Windsor Walk, London SE58AF*

*Objective:* To provide an overview of the current level of provision of methadone maintenance in eleven European Union countries.

*Method:* National Data and key informant data was aggregated to provide a national overview and 2–3 clinics were visited to describe operational procedure in each country with such services.

*Results:* There is no consistency in definition of mode of delivery of methadone treatment in different countries and there is no consistent definition of the terms “detoxification” or “maintenance” across countries. The range of provision of methadone maintenance ranges from 10 per 100,000 to 100 per 100,000. There are three dimensions of treatment, the type of drugs and formulation of drugs delivered, the mode of administration and the associated types of psycho-social treatment delivered. The styles of delivery in different countries will be reviewed.

*Conclusions:* There has been a considerable growth in methadone treatment. There is major variation in mode of delivery and style of treatment.

#### METHADONE MAINTENANCE OR WITHDRAWAL: HOW REALISTIC IS IT TO CONDUCT A CONTROLLED TRIAL?

**E.J.L. Finch, J. Strang, L. Hankinson, M. Gossop, M. Farrell, C. Taylor.** *National Addiction Centre, Institute of Psychiatry, DeCrespigny Park, London SE5 8AF, UK*

*Objectives:* A controlled trial was conducted to compare an on site daily dispensing methadone maintenance programme (MMC) with a community detoxification programme (CDT) for opiate users. The study aimed to demonstrate differential treatment effects over time on treatment retention, illicit drug and alcohol intake, HIV risk behaviour, criminal behaviour and physical and psychological health.

*Methods:* Injecting opiate users presenting consecutively for treatment who had a previous episode of treatment were randomly assigned to community drug team treatment which consisted of