be considered. Sometimes the family of the OCD patient plays an important role in maintaining the obsessive-compulsive symptoms and unless a broader approach (i.e. family approach) is applied, patients may continue to be resistant. The role of cognitive behavior therapy alone or in combination with each of these approaches is of great importance as well in these severe cases. For very severe resistant patients who do not respond to any treatment, neurosurgery may be beneficial. In the treatment of resistant cases it is important to maintain the patient's hope along with a step-by-step logical approach. This is especially true in a field that is progressing as rapidly as OCD.

S44. The economics of mental health care

Chairman: M Knapp

Abstracts not received

S45. The new generation of antipsychotics: considerations and challenges

Chairmen: T Barnes, A Altamura

MOVEMENT DISORDERS IN SCHIZOPHRENIA AND IMPLICATIONS FOR THE USE OF NEWER ANTIPSYCHOTICS

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Clinical studies of the newer antipsychotic drugs, such as clozapine and risperidone, have consistently shown a lower liability for extrapyramidal symptoms (EPS). However, the interpretation of data from controlled, comparative studies of new and conventional antipsychotics may be confounded by the issue of dosage differences, and perhaps dosage frequency. The potential lack of equivalence between the doses of the two drugs may partly explain any observed differences in side-effects. However, the development of EPS may not be simply a function of dosage. For example, while chronic akathisia may be associated with younger age and higher antipsychotic dosage, the likelihood of developing acute akathisia may be greater if high-potency antipsychotics are administered in rapidly-increasing dosage. Thus, for the newer drugs, the prescribing recommendation for a gradual introduction should mitigate against the development of acute akathisia. Similarly, for tardive dyskinesia, while the outcome may partly depend on dosage, the proportion of time that antipsychotic medication is received may be an important variable, that is, intermittent treatment may be associated with a poorer outcome than continuous treatment.

The evidence that patients developing EPS may be at greater risk of developing tardive dyskinesia, raises the possibility that the newer antipsychotics will be associated with a lower incidence of tardive dyskinesia over time. However, longer-term studies will be required to test whether maintenance treatment with new and conventional drugs at optimum doses reveals any clinically-significant differences in the incidence of this problem. Nevertheless, there are reports that clozapine may reduce the severity of tardive dyskinesia and tardive dystonia in patients that have developed these conditions while receiving conventional drugs.

DOPAMINE AND SEROTONIN RECEPTOR OCCUPANCY IN PATIENTS TREATED WITH ANTIPSYCHOTICS

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Using positron emission tomography (PET) and [11C] raclopride the mechanism of action of antipsychotic drugs was examined in schizophrenic patients treated with classical and atypical antipsychotics respectively. Regarding the *classical* antipsychotics, the dopamine hypothesis was supported by 1) the consistent finding of a high D2 receptor occupancy in patients responding to treatment with classical antipsychotics (70–90%) and 2) the finding of a statistically significant relationship between the degree of D2 receptor occupancy and antipsychotic effect in a controlled double blind study of patients treated with raclopride.

In patients treated with the *atypical* antipsychotic drug clozapine the D2 receptor occupancy was significantly lower (20–67%). It has been suggested that the atypical effects of clozapine are related to a combined effect on D2- and 5-HT2 receptors. In 5 clozapine treated patients (125–400 mg/day) examined with PET and [11C]*N*-methylspiperone ([11C] NMSP) a very high 5-HT2 receptor occupancy (84–94%) was a consistent finding. Although substantial 5-HT2 receptor occupancy has been found also during treatment with thioridazine, the combination with a relatively low D2 receptor occupancy is so far unique for clozapine.

In the new generation of antipsychotic drugs most have affinity *in vitro* both for D2 dopamine and 5-HT2 receptors. Preliminary data from four patients treated with risperidone indicates a D2 receptor occupancy of 75–80% and an even higher 5-HT2 receptor occupancy. In a study of three healthy controls given a single oral dose of 10 mg olanzapine the D2 receptor occupancy was 59–63% after 7 hours and the 5-HT2 receptor occupancy was 74–92% after 9.5 hours. The D2 and 5-HT2 receptor occupancy induced by clinical treatment with olanzapine in low doses may be similar to that of clozapine. Despite these observations the clinical significance of 5-HT2 receptor occupancy needs to be further clarified.

OLANZAPINE VERSUS HALOPERIDOL: RESULTS OF THE MULTI-CENTER INTERNATIONAL TRIAL

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This international, multicenter, double-blind, parallel trial compared the efficacy and safety of a single dose range of olanzapine, 5–20 mg/day, to a single dose range of haloperidol, 5–20 mg/day, in the treatment of 1,996 in- and out-patients with a DSM-III-R diagnosis of schizophrenia (83.1%), schizophreniform disorder (1.9%), or schizoaffective disorder (15.0%). Patients were assigned by random allocation to double-blind therapy in the ratio of 2 olanzapine to 1 haloperidol. The acute phase of the trial was 6 weeks in length which was followed by a double-blind extension. Patients who remained in double-blind treatment at least 3 weeks but were not showing