chotic disorders were examined with IBZM-Spect during neuroleptic monotherapy. Six patients received haloperidol (10 mg–20 mg), 11 patients had risperidone (5 pat. 3 mg/day, 6 pat. 8 mg/day), four patients received clozapine (400–600 mg) and three patients received the novel antipsychotic seroquel. Eight non-psychiatric individuals served as controls. Comparing S/F ratios with the control group (mean 1.64, range 1.60–1.78, sd 0.08), the ratios were lowest in the haloperidol group (mean 1.09, range 1.04–1.15, sd 0.04), followed by the risperidone 8 mg group (mean 1.18, range 1.14–1.26, sd 0.04) and the rispridone 3 mg group (mean 1.25, range 1.161.36, sd 0.05), the seroquel group (mean 1.54, range 1.51–1.56, sd 0.02) and the clozapine group (mean 1.53, range 1.44–1.64, sd 0.09). Differences between the values of the haloperidol group and the other groups and the difference between the 3 mg and the 8 mg risperidone group reached statistical significance. Our results indicate a substantially lower dopamine D2 receptor occupancy by the atypical antipsychotic substances clozapine and seroquel.

PSYCHIATRIC COST-EFFECTIVENESS OF DRUG AND COGNITIVE-BEHAVIORAL THERAPY IN SCHIZOPHRENIA

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The combination of pharmacotherapy and cognitive-behavioral therapy in schizophrenia is an important economic force to reduce the cost of the psychiatric care by reducing the risk of psychotic relapse.

The cognitive-behavioral profession provides a theoretical model to understand the drug-compliance problem in schizophrenia and to enhance its therapeutic approach.

The main components of this approach include continuous behavioral analysis, enhancement of therapeutic alliance, psychoeducation of the patient and significant others, perceptual and attitudinal strategies, behavioral strategies and cognitive restructuration.

The psychiatric cost-effectiveness of a group of drug non-compliant schizophrenics (N = 32), who received a cognitive-behavioral treatment, was compared with that of a control group (N = 32).

The data were adjusted for age, sex, duration of stay, level of psychopathological disturbance, duration of illness and diagnosis.

The results show differences in time involved in the psychotherapeutic approach and length of hospital stay after the index-admission.

The comparison illustrates a significant drop in the overall per patient cost of psychiatric care in the therapeutic group.

PET STUDY WITH THE BENZAMIDE TIAPRIDE

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Introduction: In hyperkinetic disorders like Huntington's Chorea, Tics, tardive dyskinesia and others the dopaminergic neurotransmitter system in the striatum is involved. The selective dopamine-2-receptor antagonist tiapride is wellknown as a substance with a high antidyskinetic efficacy in these indications. The study aim was to determine in vivo the capability of tiapride to block dopamine-2-receptors in the striatum in various dosages through PET analysis.

Method and Material: 8 healthy volunteers entered the study. Each volunteer underwent 2 or 3 PET scans: a baseline scan without pretreatment with tiapride and another one or two after different intervals (1 hour or 5 hours) following the oral administration of tiapride in various single doses (100 mg/die or 300 mg/die or 600 mg/die). The used radioligand was ^{11}C-Raclopride, which binds, as an antagonist, selectively to dopamine-2-receptors but not to other receptors.

Result: The following dopamine-2-receptor occupancy data (in percentages) were obtained in the study:

Tiapride dosage	After 1 hour	After 5 hours
100 mg	33%	34% (putamen)
	33%	38% (caudate n.)
300 mg	73%	78% (putamen)
	70%	79% (caudate n.)
600 mg	76% (putamen)	
	77% (caudate n.)	

Conclusion: Via PET analysis it was possible to demonstrate, that tiapride is also in vivo a powerfull dopamine-2-receptor antagonist. Initial dose/occupancy relationships could be determined.

'SEROQUEL'™ (ICI 204,636) EPS AND PROLACTIN: COMPARISON WITH HALOPERIDOL

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The atypical antipsychotic clozapine has minimal extrapyramidal symptoms (EPS) liability and does not cause sustained hyperolactinaemia. These atypical features are expected to improve compliance, reduce hospitalisations and enhance the quality of life for patients with schizophrenia. 'Seroquel' (ICI 204,636) is a promising new antipsychotic with an atypical profile. In phase II clinical trials there were no differences between ICI 204,636 and placebo in EPS as assessed by the Simpson Scale total score, use of anticholinergic medication and the incidence of motor system adverse events. Further, there were no differences between the ICI 204,636 group and placebo group in changes from baseline in prolactin (PRL) levels after 6 weeks of treatment. EPS and PRL were further assessed in a phase III multicentre, double blind, randomised comparison of ICI 204,636 and haloperidol. This trial evaluated the efficacy and tolerability of ICI 204,636 and haloperidol over a 6 week period in the treatment of patients with an acute exacerbation of chronic or subchronic schizophrenia. The patients were dosed flexibly depending on clinical response and tolerance up to 800 mg ICI 204,636 daily (221 patients) or 16 mg haloperidol daily (227 patients) both administered b.d. ICI 204,636 caused less EPS as shown by a lower incidence of motor system adverse events such as akathisia, hypertonia, EPS tremor and dystonia in the ICI 204,636 group. In addition, the concomitant use of anticholinergic drugs was less common in the ICI 204,636 group (13%) as compared with the haloperidol group (49%). Finally the majority of patients treated with ICI 204,636 had either an improvement or no change in EPS, as assessed by the Simpson Scale, whereas the majority of patients treated with haloperidol experienced a worsening of EPS (except at day 7) and there were statistically significant differences ($p < 0.05$) at all time points in favour of ICI 204,636. There was a significant difference ($p = 0.0001$) in PRL due to a decrease in the ICI 204,636 compared to an increase in the haloperidol group. These results provide further support to the hypothesis that ICI 204,636 has an atypical profile.

'Seroquel' is a trademark, the property of Zeneca Limited.

PLASMA LEVELS AND METABOLISM OF CLOZAPINE IN RELAPSE PREVENTION OF SCHIZOPHRENIA

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The atypical neuroleptic clozapine (CLOZ) is frequently used for relapse prevention in schizophrenic outpatients who developed full or partial remission under CLOZ. Unfortunately, there are no clinical studies regarding CLOZ dosage or plasma level which are neces-

sary for effective relapse prevention. Therefore, we started a study in 60 outpatients treated with CLOZ for at least one year. For determination of CLOZ and its major metabolites desmethyl. CLOZ and CLOZ-n-oxid, we used reversed phase chromatography (HPLC) and UV detection (254 nm) with imipramine as an internal standard (Weigmann and Hiemke, 1992).

A preliminary analysis of 25 patients who were treated with oral dosage between 75 and 600 mg revealed a plasma level of CLOZ at (mean ± SD) 176 ± 216 ng/ml (range 34–1038 ng/ml), desmethyl-CLOZ at 103 ± 109 ng/ml and CLOZ-n-oxide at 24.1 ± 18 ng/ml.

Separate analysis of smokers (n = 16) and nonsmokers (n = 9) suggests a relevant influence of smoking on CLOZ plasma concentration and metabolism. Mean CLOZ plasma levels were significantly lower in smokers (94 ng/ml, S.D. 68.7) than in nonsmokers (313.9 ng/ml, S.D. 125, $p < 0.01$). On the other hand, the desmethyl CLOZ/CLOZ ratio as well as the CLOZ-n-oxide/CLOZ ratio was significantly higher in smokers.

The prospective determination of CLOZ and its metabolites in patients treated for relapse prevention might be useful in order to identify (a) patients with extremely high plasma levels where the dosage can be markedly reduced; (b) fast metabolizers and/or patients who are noncompliant; (c) to evaluate the dosage necessary for relapse prevention by correlating plasma level with intraindividual relapse rates.

CLINICAL HETEROGENEITY OF DSM-IV SCHIZOPHRENIC DISORDERS

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We studied the five subcriteria of the DSM-IV diagnostic criterion A for schizophrenic disorders in a sample of 94 patients with a definite diagnosis of schizophrenia. 91 patients satisfied the first subcriterion (delusions), 62 the second (hallucinations), 22 the third (disorganized speech), 21 the fourth (grossly disorganized or catatonic behavior) and 56 the fifth (negative symptoms). From the 28 logically possible subcriteria combinations for the satisfaction of criterion A, 17 were actualized in our sample. The most frequent occurrences of combinations were those of A_1 and A_2 (25 cases), A_1 and A_5 (13 cases), A_1, A_2 and A_5 (11 cases) and A_1, A_2 and A_3 (7 cases). A cluster analysis resulted in four clusters of patients: the first (30 cases) was characterized by subcriteria A_1, A_2 and A_5, the second (29 cases) by A_1 and A_2, the third (27 cases) by A_1 and A_5 and the fourth (8 cases) by subcriteria A_1, A_2 and A_3. Our findings suggest that with the sole exception of delusions, the class of schizophrenic patients according to DSM-IV remains to a large extent heterogeneous with respect to the clinical attributes covered by the subcriteria of criterion A.

D2 DOPAMINE RECEPTOR OCCUPANCY (IBZM-SPECT) AND EXTRAPYRAMIDAL SYMPTOMS UNDER TREATMENT WITH RISPERIDONE

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We performed IBZM-SPECT in eighteen schizophrenic inpatients (DSM III R) (age range from 20 to 62 years) with a predominant negative score on the Positive and negative symptom scale (PANSS). All patients received a neuroleptic monotherapy with risperidone for at least four weeks. The mean daily dose was ranging from 0.029 to 0.128 mg/kg body weight. Plasma levels of risperidone and prolactin were also measured. PANSS-ratings were carried out on the day of SPECT examination. In addition extrapyramidal symptoms (EPMS) were assessed with the extrapyramidal symptom rating scale (ESRS). I-123 IBZM-SPECT was performed 2 hr after injection of 185 Mbq IBZM (3-iodo-6-methoxybenzamide, Cygne BV). For data acquisition a rotating three-head gamma camera (Picker Prism 3000, matrix 128×128, high-resolution fan beam collimator, filtered back projection) was used. The striatum/frontal cortex ratio of tracer binding (S/FC) was reduced in all patients treated with risperidone (S/FC = 1.72–1.02). The normal reference range of the S/FC ratio was > 1.8. The degree of D2 occupancy revealed an exponential dose-response relationship ($r = 0.9$, $p = 0.001$). EPMS of low degree were registered in 8 of 18 patients. They presented with S/FC ratios between 1.1 and 1.5. In our treatment group (daily dosage 2 mg to 8 mg) there was no dose relationship concerning EPMS. The established exponential dose-response relationship of D2 receptor blockade reflects that changes in receptor occupancy seem to be directly proportional to the amount of D2 receptor blockade. In comparison to previous studies [1] with haloperidol and clozapine the results under risperidone therapy showed an intermediate behaviour of the dose-response curve of the D2 occupancy.

[1] Scherer J, Tatsch K, Schwarz J, Oertel W, Kirsch CM, Albus M, Biol. Psychiat. 36 (1994) 627–629.

GENETIC-EPIDEMIOLOGY OF SCHIZOPHRENIA AND AFFECTIVE DISORDERS: A SURVEY ON A REPRESENTATIVE SAMPLE

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The degree of genetic implication in the etiopathogenesis of schizophrenia and affective disorders is still obscure. Genetic-epidemiology attitude towards this complex problem is a contribution to the knowledge of genetic etiology of psychiatric disorders. This representative sample consisted of 169 schizophrenic and 175 affective disorders patients. The selected patients group met ICD-9 and ICD-10 criteria. The family screening method with originally introduced genogram symbols was used. It was identified 10.6% of schizophrenic and 13.1% of affective disorders probands, with unilineal or bilineal hereditary burden. Psychiatric morbidity in their relatives was traced in at least three generations. In certain cases, regarding deceased relatives, data were unreliable. Therefore the term "undiagnosed psychiatric features" was proposed. In the schizophrenic probands families the prevalence for relatives at risk was as following: affective disorders (38.5%), undiagnosed psychiatric features (34.6%), schizophrenia (15.4%) and schizoaffective disorder (11.4%). In the affective disorders probands families the prevalence for relatives at risk was as following: affective disorders (41.0%), undiagnosed psychiatric features (38.5%), schizophrenia (15.3%) and schizoaffective disorder (5.2%). This representative sample survey suggests the psychiatric morbidity aggregation in the schizophrenic and affective disorders index patients families, indication elements for setting the role and mode inheritance in the etiopathogenesis and comorbidity of psychiatric illnesses.

HOW DOES SEX INFLUENCE UTILIZATION OF PSYCHIATRIC SERVICES IN VULNERABLE SCHIZOPHRENIC PATIENTS?

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Epidemiological studies of the past decades have shown that women utilize more frequently outpatient mental health services than do men, although prevalence rates concerning psychiatric illnesses do not differ significantly. Most of these studies refer to minor mental health problems. Recent studies focusing on women in long-term psychiatric care suggest that women have less intensive input from services and are not adequately served according to their needs.