COMPARISON OF REGIONAL CEREBRAL BLOOD FLOW IN PATIENTS WITH MAJOR DEPRESSION BEFORE AND AFTER TREATMENT USING HMPAO SPECT

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The aim of the study was to compare regional cerebral blood flow (rCBF) in patients with major depression before treatment and after recovery. Twenty patients who met the DSM-IV criteria for major depressive episode were included in the study. Participation in the study required a minimum score of 18 points on the 17- item Hamilton Depression Rating Scale. The patients were studied using HMPAO with 740 Mbq pertechnate 99 mTc. Data acquisition were carried using a single head rotating gamma camera equipped with the high resolution collimator. Regional tracer uptake was measured by a semi-quantitative method on three brain slices reoriented according to the orbito-meatal (OM) line. Each patient underwent the SPECT study twice -before treatment and after recovery. The statistical significance was analysed using the pair t-Student test.

After successful treatment, a significant improvement of tracer uptake in comparison to status during depressive episode was found. The improvement of rCBF was observed in almost all regions except right occipital region and left frontal region at level OM + 3.5 cm.

The influence of the age of the patients as well as the course of illness on rCBF will be discussed.

In conclusion, regional cerebral blood flow during major depression was markedly reduced and it improved during remission.

QUALITY OF LIFE OF SCHIZOPHRENIC PATIENTS UNDER WORK-RELATED REHABILITATION

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Quality of life (QOL) under rehabilitation has been rarely studied in psychiatry. In a cross-sectional study in 60 chronic schizophrenic outpatients (mean age 36.3 ± 11.1, 52% female) we investigated the effect of a work-oriented rehabilitation programme on the patients' QOL in comparison to a control group of patients with the same diagnosis, but without rehabilitation (waiting list). Patients of the rehabilitation group had been attending the programme for a median duration of 8.5 months. The programme focuses on occupational and everyday skills and also involves social aspects (team work etc.). The patients' QOL was assessed using two self-administered questionnaires: the Munich List of Life Dimensions (MLDL, Heinisch et al. 1991) and the Everyday Life Questionnaire (Bullinger et al. 1993), the former measuring life satisfaction, the latter functional QOL. In addition, the patients' life satisfaction (MLDL) was assessed independently by the social workers in charge.

Main results: 1) Both life satisfaction and functional QOL was increased in the rehabilitation group in the majority of domains assessed. Increase was highest for satisfaction with work, followed by leisure time activities, independence and friendships/acquaintances. Results indicate that the rehabilitation programme acts like a 'lever' which applied to *one* point (work, day structuring) subsequently affects most domains of daily living. 2) There were remarkable discrepancies between self-assessment and third-party assessment of life satisfaction, correlations being moderate for the assessments of various 'concrete' domains of life, such as social relations or leisure, but very low for the more 'abstract' items of physical and psychological well-being. Results will be discussed.

SEVENTEEN MONTHS OF POST-MARKETING SURVEILLANCE (PMS) ON TIAPRIDE ON 6792 PATIENTS

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6792 patients treated with Tiapride, a benzamide and D_2-blocking agent, were documented starting in October 1993 through to February 1995 by office-based neurologists, psychiatrists, internists and general practitioners in Germany. The scope of the PMS was to collect data on the safety and tolerance profile of tiapride. 3819 female and 2902 male patients were included (missing data of sex in 71 patients). Among these 2/3 were under and 1/3 over 75 years old. Tiapride was used for the treatment of extrapyramidal affection (36%), impaired coordination (30%) and in 11% of all cases it was administered for the treatment of side-effects due to neuroleptics and anti-parkinson drugs. Alcohol withdrawal symptoms were treated with triapride in 4.5% and psychomotor agitation in 7.5% of all cases. Most patients (95%) had received tiapride for the first time. Only 137 adverse reactions were registered in 97 patients. 1.4% of all patients reported the following adverse events in decreasing order of frequency: fatigue, dizziness and agitation. The adverse event profile reflects the pharmacological properties of tiapride and is consistent with the cumulative international experience of the drug.

BRAIN-MORPHOLOGIC CHANGES IN THE COURSE OF SCHIZOPHRENIA

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The reproducibility of morphometric measures within the same individual is a key feature to successful application of MRI technology to clinical medicine as well as to scientific research, and in particular to prospective studies evaluating the progression of brain volume loss. In view of the almost complete lack of such studies on even basic normative data, we have carried out a study with 53 healthy subjects and 13 monozygotic healthy pairs, all of whom were imaged twice at an interval of 14 days. Parallel to the MRI assessments EEG recordings were carried out at approximately the same points in time. The results of this normative study have not only provided data on the inter-individual scattering of morphometric and EEG measures in the general population, they have also enabled us to distinguish between "natural" fluctuations and "significant" changes in prospective studies with repeated assessments of the same individual. Based on the findings of a recent study of monozygotic twins discordant (N = 27) and concordant (N = 13) for schizophrenia, where evidence of non-genetic anatomical changes in the brain was present in almost every twin with schizophrenia, we have started a prospective study of 24 schizophrenic patients with repeated assessments at half-year intervals, in order to investigate the time development of brain-morphologic and electroencephalographic abnormalities over a 4-year period in young schizophrenic patients, likely to show a severe, more chronic course of illness.

IMAGING OF DOPAMINE-2 RECEPTORS WITH IBZM-SPECT IN PSYCHOTIC PATIENTS TREATED WITH TYPICAL AND ATYPICAL NEUROLEPTICS

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Twenty-nine patients with a diagnosis of schizophrenia or other psy-

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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-

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