

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  $\pm$  SD) 176  $\pm$  216 ng/ml (range 34–1038 ng/ml), desmethyl-CLOZ at 103  $\pm$  109 ng/ml and CLOZ-n-oxide at 24.1  $\pm$  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

L. Lykouras, P. Oulis, V. Tomaras, G. Christodoulou, C. Stefanis.  
*Athens Psychiatric University Clinic, Eginition Hospital*

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<sub>1</sub> and A<sub>2</sub> (25 cases), A<sub>1</sub> and A<sub>5</sub> (13 cases), A<sub>1</sub>, A<sub>2</sub> and A<sub>5</sub> (11 cases) and A<sub>1</sub>, A<sub>2</sub> and A<sub>3</sub> (7 cases). A cluster analysis resulted in four clusters of patients: the first (30 cases) was characterized by subcriteria A<sub>1</sub>, A<sub>2</sub> and A<sub>5</sub>, the second (29 cases) by A<sub>1</sub> and A<sub>2</sub>, the third (27 cases) by A<sub>1</sub> and A<sub>5</sub> and the fourth (8 cases) by subcriteria A<sub>1</sub>, A<sub>2</sub> and A<sub>3</sub>. 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

T. Mager, I. Dähne, S. Dresel<sup>1</sup>, F. Pajonk, K.H.J. TatschMöller<sup>1</sup> <AU>.  
*Dept. of Psychiatry, University of Munich, Nussbaumstr. 7, D 80336 Munich, Germany;* <sup>1</sup>*Dept. of Nuclear Medicine, University of Munich, Nussbaumstr. 7, D 80336 Munich, Germany*

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 Mq IBZM (3-iodo-6-methoxybenzamide, Cygne BV). For data acquisition a rotating three-head gamma camera (Picker Prism 3000, matrix 128x128, 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

U. Marinković, M. Nikolić, I. Timotijević. *Institute of Mental Health, Palmoticjeva 37, 11 000 Belgrade, Yugoslavia*

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?

M. Martini, W. Rössler. *Central Institute for Mental Health, J 5, 68163 Mannheim, Germany*

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.

The study presented here investigates whether women with severe mental health problems (e.g. schizophrenia) differ from men concerning their needs for care and utilization of as well as benefit from mental health care services.

**Study design:** For one year, 66 vulnerable schizophrenic patients (26 women and 40 men) were followed after discharge from inpatient care throughout the following twelve months in the highly fragmented mental health care delivery system in Mannheim area. The clinical diagnosis of schizophrenia (according to ICD-10) was confirmed by a SCAN-interview, including PSE 10, which was repeated at the end of the follow-up. For assessing the patients needs for therapeutical interventions and rehabilitation, we applied the "Needs for Care Assessment" every three months. To record the patients passage through the network of mental health care services in the community we applied the Mannheim Service Recording Sheet. It not only records each contact of patients with the services in a defined time interval (weekly) but also each treatment or care-intervention provided by the contacted services. Information was obtained continuously throughout the follow-up period.

**Results:** There were no sex-related differences in sociodemographic variables in the sample, neither did women and men differ significantly in variables concerning their illness history, such as duration, number of hospital stays, etc. Their need for care was comparable to those of the men, same as the psychopathology at the beginning and end of the follow-up. Nevertheless women showed a significantly higher utilization rate of mental health care services. They not only had a higher number of contacts, but also more interventions provided.

**Discussion:** We could not confirm that chronically mentally ill women were not adequately served. In contrast, we found an increased utilization rate of outpatient services not due to differences in the course of the disease respectively different need status or psychopathology. Possible explanations could be a lower threshold for the utilization of services or a lower threshold for the perception of psychotic symptoms and the need of therapeutic interventions.

#### FORMAL CHARACTERISTICS OF DELUSIONS

P. Oulis, V. Mavreas, J. Mamounas, C. Stefanis. *Department of Psychiatry, Athens University Medical School, Eginition Hospital, 72-74 Vas. Sophias Ave., 115 28 Athens, Greece*

We studied 13 formal clinical characteristics of delusions by means of observer-rated ordinal scales in a sample of 74 psychiatric inpatients with mainly schizophrenic or schizophreniform disorders. The interrater reliability of the scales was found to be satisfactory with the sole exception of the item-scale of congruence with the affective state. High levels of conviction about their truth and to a lesser extent lack of dismissibility and lack of resistance against them were found to be the hallmarks of delusional beliefs. The latter finding underscores the fact that contrary to obsessions, delusions are typically "ego-syntonic" subjective experiences although frequently unpleasant ones. In almost one third of the cases, delusional beliefs resulted in aggressive or violent behavior against self or others. The lack of strong inter-correlations among the scales items support the hypothesis that the concept of delusion represents various aspects of patients delusional experiences which are relatively independent of one another.

#### COGNITIVE FUNCTIONING IN SCHIZOPHRENIC SUBJECTS AND THEIR FIRST DEGREE RELATIVES

D.M. Mockler, R.M. Murray, T. Sharma. *Institute of Psychiatry, Department of Psychological Medicine, De Crespigny Park, Denmark Hill, London, UK*

The study investigated memory and intellectual functioning in both schizophrenics (N = 35) and their first degree relatives (N = 77).

The two subject groups were compared to a healthy control sample (N = 48). Memory and intellectual functioning was estimated using the Rivermead Behavioural Memory Test (RBMT) and the Wechsler Adult Intelligence Scale-Revised (WAIS-R) respectively. Significantly impaired memory functioning was evident when comparing both schizophrenic subjects and their relatives to healthy controls. Schizophrenic subjects were more impaired on tests of memory functioning in comparison to their relatives. The first degree relatives were comparable to healthy controls on tests of intellectual ability. The schizophrenic subjects were significantly more intellectually impaired than both their relatives and healthy controls. The findings indicate some evidence of a similar neuropsychological deficit in memory functioning in schizophrenics and their first degree relatives.

#### COGNITIVE DECLINE IN SCHIZOPHRENIA

D.M. Mockler, T. Sharma. *Institute of Psychiatry, Department of Psychological Medicine, De Crespigny Park, Denmark Hill, London, UK*

The prevalence and course of cognitive impairment schizophrenia remains a point of debate. Is cognitive impairment in schizophrenia a dementing process, markedly declining with age or does cognitive impairment occur in the early stages of development, possibly pre onset of schizophrenia with no further marked decline with advancing age? The study investigates memory and intellectual decline in schizophrenic (n = 83) subjects compared to healthy controls (N = 47) using the Wechsler Adult Intelligence Scale-Revised (WAIS-R), Rivermead Behavioural Memory Test (RBMT) and the National Adult Reading Test (NART) in a cross-sectional study using 5 age related cohorts (18-29, 30-39, 40-49, 50-59 and 60-69 years of age). No significant variation in memory functioning was found across the 5 cohorts for the schizophrenic subjects. However, memory functioning in the control subjects was significantly disparate with impaired performance with increasing age. This found to be related to age effects. The schizophrenic subjects showed impaired intellectual and memory functioning compared to the control cohorts. Memory functioning was not significantly variable when comparing the 60-69 year old schizophrenic/control cohorts. A significant reduction in intellectual ability was evident across the 5 schizophrenic cohorts. The findings indicate that memory functioning does not decline significantly with age in schizophrenia. The healthy subjects memory functioning becomes comparable to schizophrenic subjects between the age of 60-69 years. It is possible that impaired memory functioning in schizophrenia reaches a base level in the early years/or pre-illness and does not deteriorate significantly beyond this level with increasing age and years of illness.

#### AMISULPRIDE IN THE TREATMENT OF SUBCHRONIC OR CHRONIC SCHIZOPHRENIA WITH ACUTE EXACERBATION: A DOUBLE-BLIND COMPARISON WITH HALOPERIDOL

H.J. Möller<sup>1</sup>, S. Turjanski<sup>3</sup>, S. Turjanski<sup>3</sup>, O. Fleurot<sup>3</sup>, and the Amisulpride Study Group. <sup>1</sup> *Psychiatric Department University, Munich, Germany;* <sup>2</sup> *Inserm U302, Pitié-Salpêtrière, 75013 Paris;* <sup>3</sup> *Synthelabo, 92350 Le Plessis-Robinson, France*

Amisulpride is a substituted benzamide selective for dopamine D2 and D3 receptors without activity on other receptors. In animal studies it binds preferentially to limbic receptors, indicating a potentially low propensity to induce extrapyramidal symptoms. In previous studies amisulpride was effective in productive and deficit schizophrenia. The purpose of this multicentre, international, randomized, haloperidol-controlled, double-blind study was to compare the efficacy of amisulpride (AMI) versus haloperidol (H) in the treatment