scarce. Within the ABC Schizophrenia Study, the onset and course of schizophrenic symptoms and of alcohol and drug abuse was retrospectively investigated in a representative first-episode sample of 232 schizophrenic patients by means of the structured interview "IRAOS". Information given by relatives validated the patients' reports.

In first-episode schizophrenics the rates of alcohol or drug abuse (24% and 14%) were twice the rates compared to a matched sample from the general population. Male sex and early symptom onset were major risk factors. Drug and alcohol abuse both significantly preceded the first positive symptom — on the average by more than 5 years. But neither the onset of alcohol abuse nor the onset of drug abuse significantly preceded the first symptom of schizophrenia. Alcohol abuse usually followed it, whereas drug abuse often emerged simultaneously with the first symptom. Only in one third of the comorbid cases substance abuse seemed to precipitate schizophrenia.

## ALCOHOL USE AND ABUSE IN PATIENTS SUFFERING FROM SCHIZOPHRENIC DISORDERS IN CORFU ISLAND

P. Simatis, K. Alexandropulos, M. Tzortzopulu, V. Kavadi. *2nd and 3rd Psychiatric Departments, Psychiatric Hospital of Corfu, 49100 Corfu, Greece*

Alcoholism is frequently associated with schizophrenic disorders. Statistical analysis was conducted on the frequency of this coexistence as it is represented in the psychiatric population of the Psychiatric Hospital of Corfu during a period 3 years. For this research, a specialized questionnaire was administered for the recording of demographic and social characteristics, while the scales BPRS and BECK were used for the assessment of the psychopathology and the depression of the patients. The alcoholic schizophrenic patiens constitute the 4% percentage of the total admission of the hospital. And they are the 22% percentage of the total alcoholic treated inpatients during this period. The mean age of the inpatients was 29 years of age while a great portion (63%) of them was unmarried.

Finally we recorder the possible causes that lead schizophrenic patients to alcoholism and the effects that alcoholism has on the prognosis and the therapy of this disorder.

## SCHIZOPHRENIC PSYCHOSES AND MUTATIONS OF THE CILIARY NEUROTROPHIC FACTOR (CNTF) AND NEUROTROPHIN 3 (NT3) GENES: EVIDENCE FOR THE MALDEVELOPMENTAL THEORY

J. Thome, A. Baumer, A. Harsányi, P. Foley, J. Kornhuber, M. Rösler, P. Riederer. *Department of Psychiatry, University of Würzburg, Füchsleinstrasse 15, D-97080 Würzburg, Germany*

The maldevelopmental theory postulates that neurodevelopmental deficits, disturbances of cell migration and dysconnections of neural and glial structures are crucial factors in the etiopathogenesis of schizophrenic psychoses. Neurotrophic factors play a central role in the regulation of neural development and postnatal maintenance. For the CNTF gene, a null mutation has been described, whereby homozygote mutants lack CNTF completely, while for the NT3 gene, a missense mutation, Gly → Glu (GGG → GAG), is known. The aims of the present study were to investigate the frequencies of these mutations in psychiatric patients and to determine whether an association with schizophrenic psychoses is evident. Further, the allele frequencies were determined for the first time in a Caucasian population.

212 psychiatric inpatients (ICD-10 diagnoses) were examined with respect to CNTF mutation, of whom 188 were also examined for NT3 gene polymorphism; these genes were also examined in 60 healthy controls. Genotype determination involved extraction of genomic DNA from blood, PCR with primers flanking the gene region of interest, digestion of the PCR products with restriction endonucleases, fragment separation by gel electrophoresis and analysis under UV light. Previoulsy described primers have exhibited dimerization tendencies which interfere with genotype determination; we have therefore developed a new protocol for NT3 genotyping using more specific primers.

The schizophrenic psychosis group (n = 51) showed a significantly increased frequency of the CNTF null mutation allele when compared to healthy controls (0.250 vs. 0.122; $\chi^2$ test, $p < 0.05$). Patients with other diagnoses exhibited no increased frequency of the mutated allele. Further, the CNTF mutation was not in Hardy-Weinberg equilibrium, as there were only 7 homozygote mutants, whereas 15 would be predicted. Concerning the NT3 polymorphism, we found a frequency of 0.006 for the allele *Glu* in the total sample. There were no homozygotes (*Glu/Glu*), and the three heterozygotes (*Gly/Glu*) belonged to the patient group (2× endogenous depression, 1× hebephrenia).

Neurotrophic factor genes have been considered as strong susceptibility loci in research into the etiopathogenesis of schizophrenia. Our results suggest mutation of the CNTF gene as a genetic factor which could increase an individual's risk for schizophrenic psychosis. The detected frequency of the NT3 allele *Glu* in Caucasians is far lower than that previously described for a Japanese population reference. An association of the mutant allele with schizophrenic psychoses was neither refuted nor confirmed, but all heterozygotes suffered from endogenous psychoses. Taken together, our findings lend further support for the maldevelopment theory of schizophrenic psychoses.

## INCREASED MORBID RISK OF SCHIZOPHRENIA IN RELATIVES OF PATIENTS WITH SEVERE BIPOLAR DISORDER

V. Vallès [1], R. Guillamat [2], L. Fañanás [3], B. Gutiérrez [3], M. Campillo [4], J. van Os [5]. [1] *Dept. of Psychiatry, Hospital de Terrassa, c. Torrebonica, 08227 Terrassa, Barcelona, Spain;* [2] *Consorci Hospitalari Parc Taulí, Sabadell, Barcelona;* [3] *Dept. Anthropology, School of Biology, University of Barcelona and Catalan Institute of Public Health (ISPC);* [4] *Clínica Mental Santa Coloma, Barcelona;* [5] *Dept. of Psychiatry, University of Limburg, The Netherlands*

If "the familial liability to schizophrenia is, at least in part, a liability to develop psychosis" (Kendler et al., 1993), one would expect a higher morbid risk of schizophrenia in the relatives of bipolar disorder at the severest, psychotic end of the spectrum (Hypothesis 1). In addition, one would expect, analogous to findings in patients with schizophrenia, high familial morbid risk for schizophrenia to be associated with female gender (H2), early onset (H3) andpoor prognosis (H4).

We tested these hypotheses in a sample of 104 patients with severe DSMIIIR bipolar disorder requiring on average 6.13 admissions over 16 years. An average of 2 relatives for each proband were interviewed using the FH-RDC, and age and sex-adjusted morbidity risks were calculated according to the method of Strömgren.

H1: MR for not only bipolar disorder (5.2%), but also schizophrenia (3.0%), are much higher than reported population risks. H2/3: MR for schizophrenia in relatives of the female, early onset (below 50th percentile) group (7%) was significantly higher than in the other groups (female late onset: 1.0%; male early onset: 0.0%; male late onset: 3.1%). H4: familial morbid risk for schizophrenia, expressed as a continuous, age and sex-adjusted likelihood ratio score, was associated with the average number of hospital admissions per year (as a proxy of illness severity).

https://doi.org/10.1016/0924-9338(96)88941-3 Published online by Cambridge University Press