schizophrenic offenders were investigated with respect to psychiatric and premorbid history and circumstances at the time of the offence. They were compared to 30 non-offender male schizophrenic inpatients, of whom 23 displayed violent behaviour during the index hospitalization while 7 did not show any aggressive behaviour even in their history. Patterns of social and professional achievement were poorest in the offender group and best in the never-violent group, while non-offender violent inpatients held a medium position. Offender patients had mean 7.4 previous psychiatric hospitalizations, previous convictions in 54%, alcohol abuse in 72% and previous assaultive behaviour in 85%. Unemployment was common with 85%, all subjects derived from low social levels and predominantly lived with their parents ore alone, psychosocial stress factors in the year before the index offence were heavy or very heavy in 92%. Premorbid social adjustment, measured by the general part of the premorbid adjustment scale (PAS), was generally poor, the familiar background corresponding to the respective social level, but not generally extremely unfavourable and not characterized by habitual violence. The offender patients could be differentiated into two types: 7 patients with premorbid antisocial behaviour often were diagnosed as disorganized type of schizophrenia, were at young age at time of first psychiatric hospitalization (mean 18.4 yrs.) and index offence (mean 20.6 yrs.), had previous convictions in 100% and abused drugs in 74%. On the other hand, 18 patients without premorbid antisocial behaviour were all diagnosed as paranoid type of schizophrenia, were significantly older than the other group (mean 26.2 yrs. at first hospitalization and 36.4 yrs. at index offence) and had experienced social drift during the course of their illness. Drug abuse was rare among these patients, and all suffered from ideas of persecution or injury during the violent offence. *Conclusions:* Premorbid social adjustment, social adjustment during the course of illness as well as the illness itself play a major role in the origin of aggressive behaviour in schizophrenics. Two types of violent schizophrenics can be described with different impact of these three factors.

NR19. Psychopharmacology and substance abuse

Chairmen: I Stolerman, D Ball

ACUTE ETHANOL WITHDRAWAL IS ASSOCIATED WITH DECREASED STRIATAL DOPAMINE TRANSPORTER LEVELS?

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Dopamine levels have been suggested to play a role in alcohol withdrawal. In the present study, the effect of acute alcohol withdrawal on human dopamine (DA) transporters was investigated with SPECT using the ligand [123-I]2β-carbometoxy-3β-(4-iodophenyl)tropane([123-I]β-CIT) (MAP Medical Technologies Oy).

[123-I]β-CIT binding to striatum was examined in 12 alcoholics (mean age 42 yrs, range 32–53) during withdrawal symptoms after a period of at least 2 weeks of heavy ethanol intake (140 g/day). Controls were healthy volunteers (mean age 36 yrs, range 21–51). Most of them were getting in the acute phase a large amount of benzodiazepines, but no other psychoterapics were given. Transporter levels were examined 1–4 days after cessation of ethanol intake and after four weeks of abstinence monitored by interviews and biochemical markers (serum desialotransferrin, CDT) and by urinary screening for narcotics. The first scans were taken one and four hours (serotonin transporter density) and the third scan one day after injection of the tracer (dopamine transporter density). Transaxial slices oriented in orbito-meatal (OM) line were reconstructed and the following regions were drawn: 1) medial prefrontal cortex (MFC), 2) striatum (STR) and 3) frontal white matter (FWM). ROIs were drawn using MRI. The following ratios were calculated: 1) MFC/FWM at one and four hours (serotonin transporter density) and 2) STR/FWM at one day (dopamine transporter density).

Dopamine transporter density was significantly higher after four weeks of abstinence (8.0) compared with withdrawal situation (7.3), ($p < 0.01$). After four weeks abstinence the levels were similiar to those of healthy controls (STR/FWM = 8.0; n = 15). Both I-type and II-type alcoholics showed decreased density of striatal dopamine transporters. In contrast, no significant difference could be found in serotonin transporter density at one hour after injection of the tracer in medial prefrontal cortex (MFC/FWM) during withdrawal (1.18) and after four weeks of abstinence (1.12).

The present data indicates that decreased striatal dopamine activity may be an important mechanism of ethanol-induced withdrawal symptoms. However, the possible effect of benzodiazepines should be taken into consideration.

MDMA (ECSTASY)-ABUSE IN YOUNG ADULTS — IS THERE A RISK PROFILE FOR SEVERE PSYCHIATRIC DISORDERS?

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Introduction: There has been a considerable increase in the use of Metamphetamindervates such as MDMA in Western Europe. There exist only a few case reports on anxiety, depression and paranoia linked to MDMA in young adults.

Objectives: As a part of an epidemiological Study we tried to establish a risk profile for psychiatric disorders in so called recreational MDMA-users to be able to predict the probability of later psychiatric disorder in this group.

Methods: We examined 120 MDMA-users (mean age 17.6 y) with a semi-structured interview that had been tested in former studies. Apart from basic data it focuses on the personal ways of abuse and paranormal experiences during drug-intake and later on.

Results: 25% (n = 30) of the adolescents reported hallucinations, anxiety and depression during and after MDMA-intake and in the time afterwards. The severity and duration of the symptoms was correlated both with amount and duration of drug-intake and to its social context. All 6 patients with psychosis-like symptoms took MDMA alone, longer than six months and as a sort of self-medication against depression.

Conclusions: These first qualitative data on the risk of psychiatric symptoms in recreational MDMA-users have to be reconfirmed by larger studies, although there still are major methodological and practical problems to be solved. But combined with the knowledge about clinical cases with MDMA-related disorders there seems to be some evidence that there is a certain subgroup of MDMA-users that are at a risk to develop severe psychiatric disorders.

Further epidemiological and clinical studies on this issue have to

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be done in order to create psychiatric and public health concepts to cope with this growing problem.

COMPLIANCE WITH PSYCHOPHARMACA — CLINICAL PRESCRIPTION MAINTAINS HOW LONG?

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This work took place in a community based psychosocial centre. One of the tasks of this centre is take of care for patients after their hospitalization in a psychiatric ward. Some are motivated to come immediately after their stay, others need weeks or months to make this effort. All of them answer a questionaire, including prescription from the hospital and how long it took time until the medication was changed. It was also of interest by whom the modification was made and which motivation caused it. The questionaires of 50 patients were examined in this first step. It can be shown that there are critical times after about two or three weeks and a few (two to four) months. One of the cornerstones is the level of information offered. The more the patients know about the effects and side effects the more they get a realistic view of what is possible and can be awaited. This entails a longer staying on the medication and better compliance.

THE LATEST TREATMENT POSSIBILITY OF KORSAKOW SYNDROME WITH FLUVOXAMINE AND COGNITIV TRAINING

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The possible pathogenetic role of the serotonerg dysfunction in the alcoholic amnestic disorder suggests the authors to treat 16 Korsakow patients with fluvoxamine. After the deliriosus-confused state the clinical diagnosis was confirmed by a specific Korsakow-test. Before the beginning of the treatment with fluvoxamine, after a two-week treatment, and at the end of the fluvoxamine and cognitiv training treatment the orientation- and memory disturbances were registrated with psychometric test. The improvement of the orientation troubles and the recently acquired memory functions was significant with the fluvoxamine therapy. Authors could measure further improvement because of fluvoxamine and cognitiv training as to the recently acquired memory. The improvement was more expressed by patients, whose IQ was higher, who didn't have dementia index and who could be placed into the reversible group on the basis of the special Korsakow-test examination. Authors drow the attention to the possibility of a new drug and cognitiv training therapy by alcoholic Korsakow patients.

CRITERIA FOR CARBAMAZEPINE AND CLOMETHIAZOLE TREATMENT REGIMEN OF ALCOHOL WITHDRAWAL

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Objective: Studies with carbamazepine (CBZ) and clomethiazole in treatment of alcohol withdrawal have shown efficacy of these drugs under controlled conditions. This study was designed to evaluate effectiveness and criteria of a treatment regimen with CBZ and clomethiazole in alcohol withdrawal under clinical conditions.

Methods — Design: Exploratory, observational, prospective study. *Setting:* Detoxification unit, Dept. Psychiatry, General Medical Center. *Subjects:* 200 consecutively admitted patients, inclusion criteria: admission for treatment of alcohol withdrawal, alcohol dependence (ICD-10: 10.25), exclusion criteria: current use or withdrawal from opiates, benzodiazepines, barbiturates and other substances. *Main outcome measures:* Duration, kind, and dosage of medication, incidence of seizures and delirium tremens. *Results — Group 1:* 99 patients had a history of previous withdrawal seizures, including 30 patients with previous delirium (high risk patients) and received prophylactic CBZ treatment (fixed schedule) after admission, 8% in this group developed seizures during the fast 30 hours with magnesium serum levels < 0.7 [mmol/l] in all subjects, 59.6% received concomitant medication with clomethiazole (individualized regimen), in 9.1% development of delirium. *Group 2:* 101 patients did not have any history of seizures or delirium, 64.4% in this group did not need any pharmacotherapy, 35.6% were treated with clomethiazol (individualized regimen), 2% in this group developed seizures, in 5% development of delirium. *Conclusions:* (1) Neither fixed-schedule nor prophylactic treatment with clomethiazole or CBZ seem warranted in patients without high risk criteria. (2) Data from patient's history seem to be good criteria for indication for prophylactic pharmacotherapy and inpatient treatment. (3) Prophylactic treatment with CBZ did not prevent seizures in all high risk patients and needs further evaluation. (4) Because of cost-containment in medical care, development of criteria for inpatient treatment of alcohol withdrawal may be important.

SUBJECTIVE AND BEHAVIORAL RESPONSES AND EVENT RELATED POTENTIALS FOLLOWING COCAINE ADMINISTRATION IN SUBJECTS WITH AND WITHOUT A FAMILY HISTORY OF ALCOHOLISM

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Despite the numerous studies showing an association between a positive family history of alcoholism and a higher risk for alcoholism, there is little information on the relationship of such family history of alcoholism with a susceptibility to other drugs of abuse. In the present study, we report the differences in the P_{300} wave of the event-related potentials, and in subjective and behavioral responses after intranasal cocaine (0.9 mg/kg) or placebo in subjects with a positive family history of alcoholism (FHP) and with a negative family history of alcoholism (FHN). Fourteen FHP and 14 FHN healthy, male ocassional cocaine users provided informed consent and volunteered to participate in this study. Each subject served as his own control and was tested under double-blind conditions on two experimental sessions. Both groups were compared on the characteristics of the P_{300} wave, on the scores in the Addiction Research Center Inventory (ARCI) and in the answers to 8 visual analogue scales (VAS). FHP subjects had significantly lower amplitudes than FHN individuals on the frontal electrodes at the $t = 10$ ($p < 0.005$) and $t = 30$ ($p < 0.03$) time points, and significantly higher amplitudes on the occipital electrodes at the $t = 30$ ($p < 0.05$) and $t = 60$ ($p < 0.03$) time points. In addition, 10 minutes after cocaine administration the FHP group had significantly higher change scores on the BG and A scales (that measure euphoric states) of the ARCI. On the VAS, FHP subjects had significantly higher change scores on how good, how happy, how high, and how stimulated they felt 10 minutes after cocaine administration. These data suggest the potential use of the P_{300} a a risk marker for cocaine abuse as it differentiates between FHP and FHN subjects. In addition, the enhanced immediate subjective response to some of the reinforcing cocaine effects may explain that FHP subjects could be at a higher risk for developing cocaine abuse.

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