S41-4
FAMILIAL INFLUENCES ON IMPULSIVE BEHAVIOR: EVIDENCE FROM A TWIN STUDY

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We administered the Diagnostic Interview Schedule Version III Revised by telephone to 3,226 pairs of male twins from the Vietnam Era Twin Registry. We examined interview items for impulsivity and recklessness that reflect *DSM-III-R* diagnostic criteria for antisocial personality disorder. The heritabilities of impulsivity and recklessness were 41% and 48%, respectively. No influence from the family environment on these two variables was observed. New, more extensive data on impulsivity and related constructs are currently being collected from a random subsample of 100 twin pairs. Impulsivity is being measured as a multifaceted phenomenon in the new study. Impulsivity will be examined as an aspect of normal personality using the three scales from the Minnesota Personality Questionnaire that define the "constraint" factor: control (is reflective, careful, rational, planful), harm avoidance (avoids excitement and danger; prefers safe activities), and traditionalism (desires a conservative social environment). Impulsivity will be examined as an aspect of psychopathology using data from structured diagnostic interviews assessing attention-deficit/hyperactivity disorder and borderline and antisocial personality disorders. We will also examine cognitive/neuropsychological aspects of impulsivity using measures such as time-perception paradigm, measures of sustained attention, and related constructs. We will determine if there are significant associations among personality, clinical, and cognitive/neuropsychological aspects of impulsivity. We will also capitalize on the twin structure of the data to evaluate the extent to which genetic factors, the family environment, and the non-family environment influence the various aspects of impulsivity.

S41-5
ANIMAL MODELS

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Disinhibition of behaviour is an important factor in the concept of impulsivity. Impulsivity has to do with a differential ability to inhibit responses, and a deficit or a variation in the ability to passively avoid. In humans, impulsivity is widely occurring, both in normal individuals (extra version) and in psychiatric patients (Plutchik and Van Praag, 1995). These authors suggest that impulsivity contains a number of compounds, like risk taking and lack of control over affects. Moreover, impulsivity is regarded a trait rather than a state, indicating that it is seen as a personality characteristic instead of a transient event. Therefore, it can be hypothetized that impulsivity is mediated by "hard wired" brain mechanisms and that a generic background could be present. A reduction in serotonin neurotransmission in the brain has overwhelmingly been associated with various forms of impulsivity (Markowitz and Coccaro, 1995), including aggression and violence.

In the past I have hypothetized that the 5-HT_{1B} receptor could play an important role in the modulation of impulsiveness and aggression. 5-HT_{1B} receptor agonists (serenics) inhibit offensive aggression in a behaviourally specific way. Recently we started research using transgenic mice, including a 5-HT_{1B} receptor knockout. This animal can be characterized as "impulsive". It displays enhanced aggression, alcohol and cocaine intake, activity and reactivity to several stimuli. Telemetric studies showed disturbed circadian rhythmicity in heart rate and bodytemperature, whereas basal levels of heart rate were lower and body temperature were higher than the normal wildtype.

The 5-HT_{1B} KO-mice is presently under investigation for several aspects of "impulsivity", including delays of reward, aggression, sexual behaviour and learning capabilities.

S41-6
AN UPDATE OF PHARMACOTHERAPY OF IMPULSIVE BEHAVIOUR

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Impulsive behaviour can be observed transnosologically under various conditions and in various psychiatric disorders. Most severe forms of impulsive behaviour result in aggression and sucidial acts. Less severe forms are related to pathological gambling, uncontrolled buying, kleptomania, uncontrolled eating and drug intake.

Medicall related impulsive behaviours are occurring in various psychiatric disorders such as schizophrenia, bipolar disorder, personality disorders, alcoholism, eating disorders, OCD, GDT and dementia. The variety of occurrence of loss of impulse control suggest that pathophysiologically different neurotransmitter systems and neurocircuits maybe involved. Furthermore there are no clear boundaries between compulsivity and impulsivity. In relation to pathophysiological theories, different lines of treatment have been tried and evaluated. Impulsive and/or impulsive-aggressive behaviours have partly been attributed to a central disinhibition. Both, the possible role of dopamin and of serotonin for the pathophysiology have been suggested. In this line, there are many reports about the use of SSRI and antidopaminergic substances for the treatment of such disorders. In relation to the pathophysiology of bipolar disorders, mood stabilizers have been recommended as well. Futhermore, the use of an antiepileptic drug Plenytoin was reported. The presence of urge symptoms seem to be critical for the treatment with opioid antagonists such as Naltrexon and Nalmefene. Both seem to reduce the subjective experiences of pleasure and therefore have close connections to treatment strategies in alcoholism, such as anticraving substances e. g. Acamprosat, which could be of value too. The treatment of impulsive behaviours, after having been neglected, for a long time attach much more interest now. More carefully controlled studies with a better definition of the disturbances will be necessary

S42. Sexual dysfunction induced by psychopharmacological treatment: epidemiology, mechanisms and treatment approaches

Chairs: Z Zemishlany (IL), MD Waldinger (NL)

S42-1
SEXUAL DYSFUNCTION AND PSYCHOPHARMACOLOGY

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Controlled studies, clinical series, and case reports suggest that many commonly prescribed psychiatric drugs are associated with

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treatment-emergent sexual dysfunction. Double-blind studies have documented ejaculatory and orgasmic delay with paroxetine, fluoxetine, sertraline, amitriptyline, clomipramine, and diazepam. Clinical series suggest that most of the antidepressant drugs with the possible exception of bupropion and nefazodone are associated with sexual dysfunction. Antipsychotic agents have been reported to cause both ejaculatory and erectile problems. There have been individual case reports of spontaneous orgasm and improved erectile function on fluoxetine. Other reported sexual side-effects include both penile and clitoral orgasm and painful orgasm. Hypothesized mechanisms of action include increased activity at the $5HT_2$ and $5HT_3$ receptor, blockade of the dopamine D2 receptor, and anticholinergic activity. Clinical series relying on patient spontaneous self-report of sexual dysfunction have consistently under reported the incidence of sexual side effects.

S42-2

THE RELEVANCE OF PSYCHOTROPICS-INDUCED SEXUAL DYSFUNCTION WITHIN THE ADR VOLUNTARY REPORTING SYSTEM IN GERMANY

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The ADR voluntary reporting system in Germany is operated jointly by the Drug Commission of the German Medical Profession and the Federal Health Agency. Approximately 100,000 ADR cases are stored in our joint data bank since 1991. Among them 430, i. e. 0.45% refer to "sexual dysfunction" when using the following search arguments: impotence, decreased/increased libido, anorgasmy, premature ejaculation, ejaculation failure, erectile dysfunction, abnormal sexuality, hyperprolactinemia. Of those 30% were associated with the use of psychotropic drugs including anticonvulsants. In the majority SSRIs and neuroleptics were incriminated as causative agents. Cardiovascular agents followed by H_2-blockers and lipid lowering agents were the most frequently accused non-psychotropic compounds.

The most frequently reported event was male impotence followed by decreased libido. Phenothiazine related events were extremely rare whereas 34 cases were associated with the use of sulpiride, clozapine and risperidone. We were puzzled by the high number of priapism (n = 10) related to clozapine, - an ADR hardly mentioned in the literature. Among 41 cases of possibly SSRI-induced sexual dysfunction a surprisingly high number (28) referred to paroxetine, 10 cases were reported in the context of fluoxetine prescriptions.

Although figures from the voluntary ADR reporting system must not be used to estimate true incidence rates, the findings suggest that there is a need of more comprehensive, comparative, prospective studies in this area, e. g. by intensive monitoring systems. The great majority of these ADRs (ca. 90%) were not reported directly by the treating physicians, but by the manufacturers. Doctors should be alerted to ask for any kind of sexual disorder in drug treated psychiatric patients and report them to the Drug Commission.

S42-3

NEUROANATOMY AND NEUROBIOLOGY OF THE CENTRAL SEROTONERGIC SYSTEM IN SEXUAL FUNCTIONING

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Sexual functioning is bound to different neuro-biological areas in the central nervous system. The neuroanatomy of sexual functioning is still hardly understood. However, the study of sexual side effects of psychoactive drugs provides us with information about the different neurotransmitter systems that are involved in specific sexual functions. In general the study of sexual side effects of antidepressant medication uses rather subjective methods, such as self-rating scales, to investigate the various sexual functions. In recent years animal research provided evidence of the important role of the serotonergic system in the central nervous system for sexual functioning. In this presentation the relevance of objective methods to investigate sexual functioning will be discussed. And based on recent double-blind studies regarding the ejaculation retarding effects of various serotonergic antidepressants the neuroanatomy and importance of the serotonergic system for orgasm and ejaculation will be discussed.

(1) Waldinger MD. Use of psychoactive agents in the treatment of sexual dysfunction. CNS Drugs 1996; 6: 204–16
(2) Waldinger MD, Berendsen HHG, Blok B, Olivier B, Holstege G. Premature ejaculation and SSRI-induced delayed ejaculation: the involvement of the serotonergic system. Behavioral Brain Research 1998 (in press).
(3) Waldinger MD, Hengeveld M, Zwinderman A, Olivier B. The effect of SSRI antidepressants on ejaculation: a double-blind, randomised, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine and sertraline. Journal of Clinical Psychopharmacology 1998 (in press).

S42-4

EFFECTS OF AGENTS ACTIVE AT THE DOPAMINERGIC SYSTEM ON SEXUAL FUNCTION

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Evidence from animal and human studies suggest that the central dopaminergic system is associated with sexual desire and erectible responses. The effects of psychopharmacological agents and illicit drugs may provide a tool to clarify the role of the dopaminergic system in sexual functioning.

Most classes of antipsychotic medications affect sexual function, probably via dopamine D2 receptor blockage and/or hyperprolactinemia. In a recent study, we found that antipsychotic treatment interferred with desire, arousal (erection) and satisfaction. Orgasm was impaired to a lesser extent. Sexual desire, however, was also decreased in untreated schizophrenic patients.

In an attempt to treat these side effects, an open-label study was undertaken in 12 neuroleptic treated schizophrenic outpatients to assess the impact of co-adminstration of Amantadine, 100 mg/day, on sexual function. Amantadine provokes the release of brain dopamine from nerve endings. As expected, Amantadine improved the scores for desire ($p < 0.02$), erection ($p < 0.05$) and satisfaction ($p < 0.05$). L-deprenyl, a selective MAO-B inhibitor, is another potential option to increase brain dopaminergic transmission. The results of a double-blind study using L-deprenyl 15 mg/day vs. placebo in treated schizophrenic patients will be presented.

Cocaine, amphetamines and MDMA ("Ecstasy") are all dopaminergic agonists. Acute use can induce an increase in desire and satisfaction, while chronic abuse may induce dopamine deficiency with decreases in desire and performance. Although the effects of these substances may support the role of central dopaminergic transmission in sexual functioning, the possibility that peripheral sympathomimetic effects may alter sexual function should also be recognized.