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.

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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.

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