

P02.279**THE CARDIOVASCULAR SAFETY PROFILE OF AMISULPRIDE IN MAN: RESULTS OF AN OPEN CLINICAL STUDY**

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Background: Compared to classical neuroleptics amisulpride has been shown to be more effective in treating negative symptoms of schizophrenia. Moreover, it induces only low or negligible extrapyramidal side effects. Concerning this clinical profile it should be regarded as an atypical neuroleptic. In vitro studies indicate that amisulpride acts selectively at D₂- and D₃-receptors. Concerning its in vitro receptor profile, no significant anti-adrenergic and anticholinergic properties should be expected in vivo.

This study 1); prospectively investigated the effects of amisulpride on autonomic neurocardiac function and ECG time relations and 2); reviewed ECG data available from large pre-clinical and clinical studies of amisulpride.

Methods: In an open clinical study 49 schizophrenics underwent serial ECG recordings during a dosing-up phase of amisulpride up to a maximum dosage of 800 mg/d. To assess the effects of amisulpride on autonomic neurocardiac regulation a subgroup of these patients additionally underwent standardized measurements of heart rate variability (1) at rest and during various provocation manoeuvres.

Results: The results of the HRV study indicate that amisulpride had no anti-muscarinic properties in vivo. Under amisulpride initially untreated schizophrenics developed a reduction of both, the mean 5-min resting heart rate and LF/HF ratio, suggesting a trend towards normalization of the neurocardiac sympathovagal balance during treatment. Further ECG analysis revealed that amisulpride did not significantly influence electrocardiographic repolarization (ST-segment, T-wave morphology, mean QTc-times) and PQ-conduction.

Discussion: Taken together our data indicate that in vivo amisulpride (400–800 mg/d) is well tolerated by the cardiovascular system.

(1) Task Force Report. Heart rate variability. *Circulation* 1996; 93: 1043–65.

P02.280**TESTOSTERONE, AGEING AND COITAL ACTIVITY**

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The aim of the study was to determine the correlation between the level of testosterone and coital activity in a group of 85 healthy men, 77 patients with Klinefelter's syndrome and 55 patients with varicocele; all of them were married and aged 22–45 years. Evaluation of plasma testosterone levels revealed that its levels were significantly decreased ($p = 0.0001$) in Klinefelter's group (mean = 4.21 ng/ml) and in varicocele group (mean = 5.72 ng/ml) in comparison with healthy men (mean = 9.49 ng/ml). Coital activity was examined using a structured interview and the Sexual Activity of Men questionnaire. In subgroups aged 36 and more the subnormal values of sexual activity were found in 67% of chromatin positive men, in 36% of patients with varicocele and only in 24% of controls. Testosterone levels do not decrease significantly with age in any of the studied groups and there was no correlation between the levels of testosterone and the coital activity.

Conclusion: Plasma levels of testosterone in adulthood age don't probably play a decisive role in the decline of male coital activity in

the period between 22–45 of age. Other factors such as enzymatic, neurogenic, sociopsychogenic and especially vascular ones might be of importance.

P02.281**FUNCTIONAL MAGNETIC RESONANCE IMAGING OF REACTION TO FOOD PRESENTATION IN ANOREXIA NERVOSA**

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Food phobia is a core component of anorectic pathology and the perception of food may be as distorted as the perception of the body shape in eating disorders. Anorectic patients differ as to the kind of feared food, energetic value being not necessarily the decisive quality. That is why we decided to select the kind of presented food individually.

8 anorectic inpatients and 4 healthy controls were asked to choose one colour picture of food, they would feel comfortable to eat, and one colour picture of food, they found unpleasant or detestable. Then functional magnetic resonance imaging was performed, using the BOLD technique, while the food pictures were presented with an accompanying instruction to think of eating the food. In an easy paradigm watching the picture alternated with looking at an empty wall. T2* EPI images were collected. Transfer into a PC enabled computation. T1W transversal images served for precise pixel to pixel transfer of the results in colour. EDI questionnaire and subjective scales were used to specify the individual eating attitudes and immediate feelings at the moment of food presentation. In anorectic patients results suggest generally more activation with picture of unpleasant food. Cortical activity was detected in frontal lobes, more often left than right, with anterior cingulate gyrus often involved in both groups. Occipital cortical activity mirrored visual perception of the paradigm. Occasional presence of activation was detected in basal ganglia, insula and hippocampus, more often left than right. The considerable variability of results among both patients and controls implies the need for larger sample studies with further improvement of the paradigm and effective motion artefact elimination.

P02.282**THE PREVALENCE OF DEPRESSION IN THE CZECH REPUBLIC**

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Depressive disorders represent a considerable economical, health and social burden for patients as well as for the whole society. In last decades the prevalence of depression has increased. In November 1999 a study was conducted to investigate 6 month prevalence of depressive symptoms in a representative sample of the Czech population and to map their intensity and quantify their consequences. The study used the DEPRES methodology. 1248 respondents aged over 15 years were assessed by structured interview focused on pathological mood changes, their impact on daily activities, suicidal thoughts, contact with health professionals and social status. Results showed that 33% of the sample met the DEPRES criteria for depression, mostly severe depression (16%). Secondly, we found the depressive symptoms in 14% of respondents and mild depression was found in 3%. Most frequent depressive symptoms were found in the cohort of 35–44 years of age. Aider 65 years the prevalence increased again. Women

suffered from the depression more frequently than men, as expected. "Depressive people" contacted physicians more frequently, and sick leaves are significantly longer than in none-depressive population. This study showed that only a small amount of affected persons have been adequately treated for the depression. Life-long prevalence of suicidal thoughts was 4.8%. Also, the social impact of the illness and stratification in population subgroups was demonstrated

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THE RELATIONSHIP BETWEEN ASPECTS OF TRAIT IMPULSIVITY AND IMPULSIVE SUICIDAL BEHAVIOR

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a) The ability to control one's thoughts and behavior is an essential personality trait which is described by the dimension of impulsiveness. Impulsivity is frequently used to classify special features of suicidal behavior. The question remains to be clarified in what way suicidal acts are influenced by cognitive and behavioral subtraits of impulsivity which can be measured by means of performance tests and personality questionnaires.

b) 45 patients with at least one suicide attempt in their history were included into this study. An additional criterion was the absence of a neurological and psychotic symptoms, addictions to a substance and other comorbidity. Subjects were diagnosed according to DSM-III-R and classified into a high and a low impulsive subgroup by means of the items No.6 and 15 of the Beck Suicide Intent Scale. A neuropsychological test battery was administered to assess speed and accuracy of cognitive performance, problem solving and time estimation. Behavioral trait impulsivity, temporal structure and time perspective were measured by standardized self report.

c) The statistical comparison of the subgroups indicate a larger number of steps for the strategic problem solving task ($p < 0.5$) in subjects with a more impulsive suicidal behavior. The high impulsive subgroup shows a decreased speed ($p < 0.5$) with a non-significant tendency of a higher error rate in a task which requires visual-motor coordination. Concerning time estimation we found inhomogeneous results. Subjects with rather impulsive suicidal features report a lower temporal structure ($p < 0.1$) as well as a higher ($p < 0.5$) present fatalistic time perspective. They also non-significantly tend to feel a lower future orientation and a higher past negative orientation. These characteristics are correlated to self-reported behavioral impulsivity ($p < 0.5$) in the whole group.

d) The preliminary results suggest the existence of a subgroup of suicidal patients in which the tendency to act on impulse within suicide attempts may be influenced by distinctive cognitive and behavioral features related to trait impulsivity. The study is ongoing to confirm these trends of significance.

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TRANSGENIC MICE OVEREXPRESSING BRAIN HUMAN AMYLOID PRECURSOR PROTEIN SHOW AN AGE-DEPENDENT COGNITIVE IMPAIRMENT IN THE MORRIS WATER MAZE

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Alzheimer's disease (AD) pathology is characterized by an increased amyloid content in the brain and by a progressive decline of cognitive abilities. A mice model of AD, transgenic mice overexpressing the 751-amino acid isoform of human amyloid precursor protein (APP) responsible for Alzheimer - like brain pathology were tested in a battery of cognitive spatial tasks and the results were related to age and sex. Tests in a modified Morris water maze (MWM) and on a stable or rotating circular dry arenas were performed in wild type mice (WT) of the JU strain and in F10 and F15 pedigrees of two different transgenic founder mice in animals aged 1.5, 3, 6 and 24 months. The animals were trained in 6 daily sessions, 4 swims/session, to find a hidden escape platform in the center of the SW quadrant of the pool in less than 1 min. In the dry arena, the animals were trained under two different conditions - in a passive (when the arena was stable) and an active (when the arena rotated 1 turn/min) place avoidance tasks. The mouse was punished by a horizontal blast of compressed air whenever it entered a prohibited 60°-sector (PS) defined in room coordinates. Four parameters were evaluated: (1) the time to the first entrance into the PS, (2) the time between two subsequent entrances into PS, (3) the total number of entrances into PS and (4) the total time spent in the PS. In the MWM, the WT animals improved in solving the task. 1.5-month old animals decreased their escape latencies significantly ($p < 0.01$) from the value of 35 ± 4 s (mean \pm s.e.m.) to the asymptotic level of 13 ± 3 s on Days 3 to 6. The asymptotic escape latencies of WT increased slightly with age. Young F15 pedigrees also improved their performance, their escape latencies decreased significantly from the initial values of 55 ± 6 s to 18 ± 2 s and 24 ± 3 s in 1.5 and 3 month old animals, respectively. These young transgenic animals improved more slowly than WT but eventually they reached the level of WT. In contrast, 6-month and older transgenic animals did not reach the WT level at all; their asymptotic escape latencies significantly differed from that of WT. In both dry arena tasks, the performance of all animals improved with training in all parameters, but there were no significant differences between groups. The discrepancy between MWM and dry arena results is under investigation. The present data demonstrate an age dependent impairment of navigation learning in MWM in mice overexpressing human APP. A slight cognitive deficit appears already in young animals and can be compensated by further training while this deficit is severe in 6-month and older animals and remains irreversible despite of extended training.

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