

craving substances. Furthermore new approaches in the psychotherapy of people with alcohol problems will be outlined. Hereby we focus on technique and evidence based efficacy of Brief Interventions. The participants will be invited to an interactive style of learning and discussing. Examples of case vignettes can be presented to illustrate early diagnosis and intervention including modern techniques such as motivational enhancement therapy (MET), cognitive behavioural therapy and dialectic behavioural treatment according to M. Linehan.

Tuesday, April 5, 2005

O-09. Oral presentation: Substance-related disorders

Chairperson(s): Mats Berglund, Ulrich Preuss (Greifswald, Germany)
16.15 - 17.45, Holiday Inn - Room 7

O-09-01

Genetic variants of the glutamate system and their role in alcohol dependence withdrawal

U. Preuss. *Johanna-Odebrecht-Stiftung Psychiatry, Greifswald, Germany*

Objective: Upregulation of glutamatergic neurotransmission resulting from chronic ethanol intoxication may cause a hyperexcitable state during alcohol withdrawal which may lead to seizures and delirium tremens. The aim of our study was to evaluate the association between a history of alcohol withdrawal-induced seizures and delirium tremens, and a number of polymorphism of candidate genes of the glutamate system (Kainate GRIK 3, NMDA GRINR2A, mGluR5, 7, 8, Glutamate transporter EAAT1) in a sample of well-characterized alcoholics compared to controls.

Methods: 291 patients meeting DSM-IV alcohol dependence criteria and 611 controls, all of German descent, were investigated. Polymorphisms of candidate genes were determined using PCR (Polymerase Chain Reaction) of lymphocyte DNA. Characteristics of alcohol withdrawal, including delirium tremens and seizures, were obtained using the SSAGA (Semi-Structured Assessment for the Genetics of Alcoholism).

Results: A number of significant relationships between genetic variations of glutamatergic genes with alcohol withdrawal (EAAT1, mGluR5, GRIN2A) and delirium tremens (GRIK3) were detected.

Conclusion: The results are suggestive for a significant role a profile of glutamatergic gene variants increasing the risk for alcohol withdrawal and its complications. However, further investigation of the variant's pathophysiological role is warranted.

O-09-02

Neuroendocrinology of alcohol seeking behaviour, craving and relapse

F. Kiefer, K. Wiedemann. *University of Heidelberg Central Inst. Mental Health, Mannheim, Germany*

Objective: Alcohol intake is known to modulate plasma concentrations of neuroendocrine peptides. However, recent results suggest that the endocrine system may not only respond passively

to alcohol intake, but that -vice versa- it also actively modulates alcohol intake behaviour.

Methods: Review of recent data on neuroendocrine aspects of alcohol addiction.

Results: The most coherent body of data concerns the hypothalamo-pituitary-adrenocortical (HPA) axis, with low corticotropin releasing hormone (CRH) being associated with more intense craving and increased probability of relapse after acute detoxification. Leptin, β -endorphin and ANP, which indirectly regulate the HPA system, also may modulate the intensity of craving or the intensity of the alcohol withdrawal syndrome.

Conclusion: Although most of the currently available data demonstrates association rather than causality between neuroendocrine changes and alcohol-related behaviours, they do provide testable hypotheses and open up perspectives of treating alcohol dependence via manipulation of the neuroendocrine axis.

O-09-03

Longterm follow-up of 180 chronic alcoholics during and after comprehensive integrated outpatient treatment: Relation of deterrent medication and outcome

H. Krampe, S. Stawicki, T. Wagner, C. Bartels, C. Aust, E. Ruether, W. Poser, H. Ehrenreich. *MPI for Experimental Medicine Clinical Neuroscience, Goettingen, Germany*

Objective: (1) To perform 9-year follow-up of abstinence, lapse and relapse in 180 chronic alcoholics who participated in the Outpatient Longterm Intensive Therapy for Alcoholics (OLITA); (2) To investigate the role of supervised DM intake in relapse prevention and as an adjunct for maintenance of longterm abstinence.

Methods: This prospective open treatment study evaluates longterm course of drinking outcomes and DM use of 180 chronic alcoholics consecutively admitted between 1993 and 2002. Subsamples are compared regarding (1) placebo-DM versus verum-DM (disulfiram/calcium carbimide), (2) coped lapses versus finally detrimental lapses versus malignant relapses, (3) DM use for 13-20 months versus DM use for > 20 months.

Results: During 9-year follow-up, cumulative probability of not having relapsed was .52, of not having consumed any alcohol .26. Despite longterm use, disulfiram/calcium carbimide were well tolerated. Patients on placebo-DM showed higher cumulative abstinence probability than patients on verum (S=.86 versus S=.49, $p=.03$). Successfully coped lapses occurred later than detrimental lapses and malignant relapses ($p<.001$); patients with coped lapse had more days of DM intake and more subsequent days without DM than patients with detrimental lapse and with malignant relapse ($p<.001$). Cumulative abstinence probability was S=.75 for patients with longterm intake compared to S=.50 for patients who stopped DM between months 13 and 20 ($p<.001$).

Conclusion: The abstinence rate of over 50% strongly supports the concept of comprehensive, longterm outpatient treatment of alcoholics. Supervised, guided intake of DM, also over extended periods, can be employed as a predominantly psychologically acting pivotal ingredient of successful alcoholism therapy.

O-09-04

Alcohol abuse among adolescents and its socio-economic parameters

I. Licanin, A. Redzic, J. Delilovic, M. Spremo. *Psychiatric Clinic University Hospital, Sarajevo, Bosnia and Herzegovina*

Objectives: It is well known that drug abuse is common in early adolescence, with almost the same epidemiological characteristics in both economically developed and undeveloped countries. Bosnia and Herzegovina, a country with postwar society, currently going through a transition period. Therefore, various risk factors related to alcohol and other kinds of substance abuse, like social, economic and health factors can be found here. Youngsters like to experiment with risky life styles, without adequate knowledge about long-term health effects. The aim of this study is to show socio-economic factors relating to alcohol abuse among adolescents and to describe parental and peer influence to adolescents behaviour.

Methods: The research focused on 600 adolescents (400 in Sarajevo Canton and 200 in Tuzla Canton – in both their rural and urban parts). This group is of an equal gender and age distributions. The research tool used was Q 2000. EPI info was used for statistical analyses. Study design is prospective, epidemiological and analytical. Results were compared within the groups, between the Cantons and between the groups.

Results: The results show that better socioeconomic life condition is directly related with alcohol abuse. It was obvious that parental passive support (>50%), and peer pressure have a strong relation to adolescents behaviour.

Conclusion: these results could be used to develop an appropriate prevention strategy. It is necessary to be aware of all relevant risk factors.

O-09-05

A comparison of Swiss and U.S. substance use disorder treatment programs: The effect of treatment characteristics and comorbid psychiatric disorders on one-year outcomes

F. Moggi, A. Giovanoli, R. H. Moos. *University Hospital Clinical Psychiatry, Bern, Switzerland*

Objective: The purpose of the study was to compare treatment characteristics of Swiss and U.S. inpatient alcohol use disorder programs, to evaluate their relationship to the patients' outcome at one-year follow-up (e.g., substance use, psychiatric symptoms, work and re-hospitalization), and to determine whether psychiatric comorbidity (e.g., alcohol use and anxiety disorders) is a moderator of this relationship.

Methods: The multicenter study utilizes a prospective, comparative, and naturalistic design, capitalizing on the two countries' realistic treatment selection and characteristics of established programs. Overall, 791 patients of twelve Swiss programs, 3'699 patients of 15 U.S. programs, and 542 therapists participated in the study. Nearly 50% of Swiss patients and 35% of U.S. patients were diagnosed with a comorbid psychiatric disorder. Using the same measurements, countries' treatment characteristics were directly compared by t-tests. Hierarchical linear and logistic regressions with treatment characteristics and psychiatric comorbidity as predictors were used to evaluate the comparative improvement of Swiss and U.S. patients' outcome.

Results: The two countries differ in treatment characteristics (all $p < .001$) such as intensity (e.g., length of stay: CH = 116 vs. USA = 25 days!), understanding of etiology (e.g., disease model), treatment orientation (e.g. cognitive-behavioral goals and interventions), self-help group participation (e.g., AA/12-Step) or ward atmosphere (e.g., structure and order). Nevertheless, most treatment characteristics were not clinically significant associated with outcome (e.g., length of stay and one-year abstinence, $r = .01$, $p = .669$; 40% abstinence

rate in CH and USA). In addition, psychiatric comorbidity is only slightly related to outcome such as work and re-hospitalization but strongly with psychiatric symptoms.

Conclusion: Although treatment characteristics and psychiatric comorbidity are statistically related to improvement of patients attending Swiss or U.S inpatient alcohol use disorder programs, their clinical relevance are rather small.

O-09-06

Anxiety and dissociative symptomatology in substance abuse disorders

M. L. Figueira. *Faculty of Medicine Dep. of Psychiatry, Lisbon, Portugal*

Objective: A number of works has pointed out the high prevalence of dissociative symptomatology in many psychiatric conditions such as substance abuse disorders, including alcohol (Good, 1989), (Wenzel, et al, 1996). The purpose of this investigation is to study comparatively the frequency and type of dissociative experiences in alcoholic patients v.s. normal controls – and correlate the level and type of dissociative experiences in the alcoholic sample with anxious symptomatology. We also intend to correlate dissociative symptomatology with demographic variables and chronicity of illness

Methods: To assess the dissociative symptomatology we applied the Dissociative Experiences Scale (Bernstein and Putnam, 1986) to 36 subjects of: alcoholic patients and 30 normal controls. Three types of dissociative experiences were examined: amnesia, depersonalization/desrealization and absorption. Level of anxiety was assessed through the Hamilton Anxiety Rating Scale (HARS). Chronicity of illness -criteria of ASI Addiction Severity Index (Mac Lellan et al., 1980) was collected. Statistical tests: t-Student, ANOVA, Kruskal-Wallis and Pearson Correlations

Results: Results agree with previous studies reporting higher levels of dissociation in alcoholic patients ($26,2 \pm 15,5$) when compared to normal controls ($3,7 \pm 2,7$) ($p < 0,001$). Alcoholic patients showed a mean value of $18,9 \pm 7,4$ in the Hamilton Anxiety Rating Scale (HARS). We didn't find a correlation between anxiety levels and prevalence of dissociative experiences in this sample (Pearson, $p = 1,125$). Chronicity of illness had a positive correlation with the DES total score (Pearson, $r = 0,459$, $p = 0,005$) and the three sub-scales in the alcoholic sample

Conclusion: Data support the hypothesis of a neurochemical basis for dissociative processes in substance abuse patients. A systematic study of a possible correlation between anxiety and dissociative symptomatology will be necessary

O-09-07

Schizophrenia following cannabis-induced psychosis: Follow-up study of 535 incident cases

M. Arendt, P. Munk-Jørgensen. *Aarhus University Hospital Basic Psychiatric Research, Risskov, Denmark*

Objective: Cannabis-induced psychosis is a controversial diagnosis. While numerous studies have shown that cannabis can induce short-lived psychotic symptoms, it is not documented what happen to the patients subsequently. Nevertheless there is general agreement in the existing literature that cannabis-induced psychotic symptoms are harmless phenomena that resolve rapidly and with complete remission. However, previous studies are limited by

severe methodological problems, out of which the lack of follow-up data is the most important. This study establishes to what degree cannabis-induced psychotic conditions are followed by schizophrenia spectrum disorders, and investigates the timing of onset of the more severe disorders.

Methods: Using The Danish Psychiatric Central Register patients admitted with cannabis-induced psychotic symptoms were identified and followed for 3 to 8 years. All subsequent diagnoses were analysed. Subjects registered with psychotic symptoms of any type before the cannabis-induced psychotic symptoms were excluded.

Results: 535 individuals with no previous history of psychosis had been admitted with cannabis-induced psychotic symptoms to Danish psychiatric departments between 1994 and 1999. A very high proportion (44.5%), was subsequently re-hospitalized with schizophrenia spectrum disorders. Onset was delayed in most instances, and 47.1% received a schizophrenia spectrum diagnosis more than a year after the cannabis induced symptoms.

Conclusion: Cannabis-induced psychotic conditions are not harmless. They are extremely important risk factors for development of long-term psychotic conditions. The onset of more severe psychopathology is generally delayed.

O-09-08

How social and biological factors impact the formation of relationship of young population to the usage of psycho-active substances in Chechnya

M. Dalsaev, Q. Idrisov, R. Dalsaeva. *Drug Addict Hospital, Grozny, Russia*

Objective: Social rocks in Chechnya reflected on some traditions and customs of ethnoses. Stratification of population and migration processes had additional psycho-traumatic impact. It might be told on relationship of population toward usage of psychoactive substances (farther PAS) among of youths. During last years stable growth of PAS usage was registered. The goal of current research was study the tendency of interests of youths in Chechnya within a context of acceptability of PAS usage including females as predictor of drug addiction and alcoholism.

Methods: Research was carried out within dynamic of last three years (2001–2004). Age of respondents was within a range of 16 up to 30 years. The total number of examined persons formed 2580 persons.

Results: It was unexpected to discover the acceptability of usage of alcohol and smoking among of youth group within the age of 16–20 years, where females more frequently used to try alcohol and males mostly tried cigarettes.

Conclusion: Among of factors exerting a vital influence upon admissibility of PAS usage, the stress factors, migration processes, and age were underlined.

O-09-09

Mortality in the offspring of people admitted for psychiatric treatment: A population-based cohort study with 26 years follow-up

R. Webb, K. Abel, A. Pickles, P. B. Mortensen, L. Appleby. *University of Manchester Division of Psychiatry, Manchester, United Kingdom*

Objective: To estimate relative risks for all-cause mortality by offspring age and parental diagnosis, and according to maternal versus paternal disorder and two versus one affected parent.

Methods: A whole population cohort of all singletons born in Denmark during 1973–1998 (N=1,459,274) was linked to a national register of all psychiatric admissions since 1969, with exposure status classified according to parental first admission dates. Relative risks were modelled using Poisson regression.

Results: Significantly increased mortality risks in offspring of parents admitted for any diagnosis were observed throughout the 26-year follow-up period, except for ages 5–15 years. Several high-risk groups, with relative risks of between two and four, were identified; i.e. neonates exposed to maternal affective disorders, and neonates and postneonates exposed to maternal alcohol & drug-related disorders. These relative risks were significantly raised compared to those for all other maternal disorders. The highest relative risks were associated with dual diagnosis. The effects of paternal disorders were generally weaker compared to maternal disorders. The postneonatal death rate was approximately doubled in offspring of two versus one affected parent.

Conclusion: The greatest number of excess deaths were attributable to alcohol-related disorders, this being the most prevalent diagnostic group in fathers and the second most prevalent in mothers. Some findings were unexpected; there was no evidence that mortality risk among offspring of parents with schizophrenia-spectrum disorders was significantly greater than for other psychiatric diagnoses, whereas relative risks for neonatal mortality associated with maternal affective disorders were markedly raised. Future analyses will investigate cause-specific mortality.

O-09-10

Cognitive dysfunction in pathological gamblers

D. Marazziti, L. Vivarelli, F. Mungai, M. Catena. *Universita di Pisa, Pisa, Italy*

Objective: Pathological gambling (PG) is an impulse-control disorder, characterized by persistent and maladaptive gambling behaviours, with disruptive consequences on familial, occupational, and social functions. Although the pathophysiology of PG is unclear, probably it represents the result of the interplay between individual (biological and/or genetic) and environmental factors. Different hypotheses have been put forward: a genetic vulnerability mainly involving dopamine receptors, biochemical dysfunctions at the level of serotonin and of dopamine systems, or even dysfunctions of distinct brain areas. Our study aimed to evaluate the possible involvement of different brain areas in PG by means of a battery of neuropsychological tests. Materials and methods Twenty outpatients (15 male, 5 female, mean age: 26+4 years) with a diagnosis of PG according to DSM-IVR criteria and 20 healthy subjects (10 male, 10 female, mean age 23+3 years) were recruited. None suffered from any severe physical illness nor had ever taken psychotropic drugs except for two patients who had occasionally taken benzodiazepine for sleep problems. The mean score for PG at the Yale Brown for Obsessive Compulsive Disorder, modified for PG (Y-BOCS-PG) was 30+2. A battery of neuropsychological tests was administered: Wisconsin Card Sorting Test (WCST) to assess the abstraction ability and the ability to shift cognitive strategies in response to changing environmental contingencies; the Wechsler Memory Scale revised (WMS-R) to provide global values for general, verbal and visual short-term memory and for long-term memory; and the FAS test which evaluates the ability to produce fluent and spontaneous language without unnecessary pauses or inability to find more

appropriate words. Results The PG patients showed different alterations at the WCST as compared with healthy subjects. There was a great difficulty to create alternative methods of problem-solving, the patients decreased instead of increasing the efficiency during the consecutive phases of the test, that is, they could not exploit the learning as a positive reinforcement. On the contrary, the mean score at the WMR-S was 97 (within the normal range) and the FAS average score was $P=27$ (normal value >20): this means that the basic language of the subjects and their ability of communication were within the normal limits. Discussion and conclusions Our findings showed that patients affected by PG showed sufficient intellectual, linguistic and normal visual-spatial abilities. On the contrary, they presented different abnormalities at the WCST. Because the WCST is sensitive to damage on the dorsolateral portion of the prefrontal cortex, as well as to damage of non-prefrontal cortical regions connected to the prefrontal cortex, our data would suggest a generalized frontal lobe cognitive deficit. Our results would seem to confirm an altered functioning of the prefrontal areas which would determine a deficit in the executive functions; this could represent a factor of vulnerability for the development of impulsive and/or compulsive behaviours, such as PG.

Sunday, April 3, 2005

P-01. Poster session: Substance-related disorders I

Chairperson(s): Karl Mann (Mannheim, Germany), Ulrich Preuss (Greifswald, Germany)
11.15 - 12.15, Gasteig - Foyers

P-01-01

Neuroimaging in alcoholism: Voxel-based-morphometry shows correlation of cingulate and frontal lobe atrophy with lifetime drinking history

A. Diehl, A. Jatzko, G. Ende, H. Welzel, T. Demirakca, K. Mann.
CI of Mental Health Addictive Behavior, Mannheim, Germany

Objective: Brain atrophy is well documented in alcoholism. Morphometric MRI studies have shown alcoholic brain alterations mainly focused in the frontal cortex and the cerebellum. But classical MRI-based volumetry requires segmentation of a priori region of interest.

Methods: To determine a detailed distribution of brain atrophy in relation to lifetime alcohol consumption we measured volumetric brain alterations in alcoholics shortly after withdrawal and in healthy social drinkers. MRI studies were performed on a 1.5 T Siemens Vision system. Structural T1-weighted 3D mprage datasets with a resolution of 1 mm^3 were obtained from 48 alcoholics (27m, 21f) and 36 healthy social drinkers (23m, 13f). Postprocessing of the images was performed using Matlab and SPM2. Volumetric evaluation was performed with Voxel-Based-Morphometry (VBM) that does not require a priori regions of interest and fits especially for cross-sectional examinations.

Results: We found regional grey matter atrophy correlating with the lifetime drinking history (LDH) only in the cingulate and in the frontal lobe ($p=0.05$) in alcoholics and healthy controls.

Conclusion: VBM give information about localized morphologic changes, indicating that there is an alcohol related brain atrophy in distinct areas correlating to alcohol consumption in alcoholics and healthy social drinkers.

P-01-02

Alcohol craving and the A1 allele of the D2 dopamine receptor gene

E. Pinto, P. Gorwood, J. Reggers, D. Vaira, S. Fuchs, W. Pitchot, M. Ansseau. *University of Liege Psychiatry, Liège, Belgium*

Objective: Significant association has been reported between the D2 dopamine receptor (DRD2) minor Taq 1A (A1) allele and substance misuse, while dopamine hypo functioning seems as well involved in substance craving. In contrast, the putative link between the A1 allele of the DRD2 and alcohol craving has seldom been studied. Our goal was to determine whether an association could be found between those parameters in alcohol dependant patients.

Methods: 60 male DSM IV alcohol dependant patients between 18 and 65 years of age were included. They were hospitalized for withdrawal and given diazepam for 8 days while all other drugs were stopped. Alcohol craving was monitored weekly throughout their 4-week stay and twice in 2 months after they were discharged, using the Obsessive Compulsive Drinking Scale (OCDS). Genomic DNA was extracted from peripheral leukocytes. Polymerase Chain Reactions (PCR) amplifying Taq 1 polymorphisms of the DRD2 were performed. The impact of DRD2 (A1 or A2 alleles) on alcohol craving was assessed by ANOVAs.

Results: While the A1 allele of the DRD2 didn't influence OCDS scores during the hospitalization, a statistically significant difference was found two months after discharge between carriers and non carriers of the A1 allele. Patients with the A1 allele (whether hetero or homozygous) exhibited higher OCDS scores than homozygous patients for the A2 allele (5.81 ± 5.06 versus 0.3 ± 0.67 , $F = 12.262$, $p = .004$). This difference was also observed with the Obsessive Thinking subscale of the OCDS (3.8 ± 3.34 versus 0.2 ± 0.42 , $F = 12.103$, $p = .004$) and with the Compulsion subscale of the OCDS (2.0 ± 1.87 versus 0.1 ± 0.31 , $F = 10.499$, $p = .006$).

Conclusion: Alcohol craving may be influenced by genetic differences in alcohol dependant patients both in its obsessive and in its compulsive components. However, carrying the A1 allele of the DRD2 increases craving only when patients are no longer hospitalized, suggesting that this influence is exerted on individuals subjected to usual drinking cues they didn't experience during their hospitalization.

P-01-03

Asialotransferrin: A poor biomarker of alcohol abuse

R. Schwan, F. Legros, V. Nuyens, L. Malet, I. Chéreau-Boudet, P. M. Llorca. *University Hospital Psychiatry B, Clermont-Ferrand, France*

Objective: The spectrum of alcohol use disorders covers hazardous use, alcohol abuse and alcohol dependence. A recent study reported that asialotransferrin, a newly proposed biomarker, offers the best discrimination between moderate and abusive alcohol consumption. However, the 'alcohol abusers' in this study were probably inadequately identified. The present study thus evaluated the performance of asialotransferrin in detecting alcohol abuse and alcohol dependence.