increasing concentrations of alcohol (24 h: 21–162%; 48 h: 76–182%; 72 h: 36–111%). In conclusion, alcohol exposure caused maximum cell death at 48 h, with cells showing some recovery by 72 h. These findings highlight the importance of hepatic bioenergetic function and the involvement of the alcohol dehydrogenase pathway in the early stages of ALD.

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EFFECT OF GLUTAMINE-CONTAINING DIPEPTIDES ON THE LEVELS OF BRAIN TISSUE AMINO ACIDS DURING ACUTE ALCOHOL INTOXICATION IN RATS

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The effects of glutamine and the glutamine-containing dipeptides, l-alanyl-l-glutamine and glycyl-l-glutamine on free amino acids were studied in the different regions of rat brain during acute alcohol intoxication. Adult male Wistar rats were used. The acute ethanol intoxication was induced by a single i.p. injection with 20% w/v ethanol solution at a dose of 3.5 g/kg body weight. Control animals received saline. l-glutamate (146 mg/kg), l-alanyl-l-glutamine (216 mg/kg), glycyl-l-glutamine (203 mg/kg) or an equivalent volume amount of saline was injected intraperitoneally 5 min before the ethanol injection. Rats were decapitated after 30 min following ethanol administration. Amino acids were measured by HPLC/CD in the large hemispheres, brain stem and cerebellum. During acute ethanol intoxication, the rat brain structures showed a considerable imbalance among neurotransmitter amino acids. The glutamate levels were significantly decreased in the large hemispheres, brain stem and cerebellum, whereas the aspartate concentrations were diminished only in the brain stem. On the contrary, the GABA level was elevated in the large hemispheres and cerebellum. The amino acid imbalance during acute ethanol intoxication was most marked in the brain stem. Glutamine, l-alanyl-l-glutamine and glycyl-l-glutamine significantly decreased the raised brain GABA levels and increased glutamate and aspartate concentrations to normal values. The results obtained show the ability of l-glutamine and its dipeptides to normalize the levels of both excitatory and inhibitory neurotransmitter amino acids in the hemispheres, brain stem and cerebellum of rats during acute alcohol intoxication. We showed previously that these compounds significantly decreased the severity of ethanol withdrawal in rats, normalized neurotransmitter amino acid levels in various brain regions during alcohol withdrawal, and diminished the voluntary ethanol consumption in rats. These findings suggest that glutamine and glutamine-based dipeptides might possess some therapeutic benefits in treatment for alcohol-use disorders.

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P50

DRD2 TAQIA POLYMORPHISMS ARE ASSOCIATED WITH PERSONALITY TRAITS THAT CORRELATE WITH ALCOHOL CRAVING IN ALCOHOL-DEPENDENT SUBJECTS

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Dopaminergic neurotransmissions play indispensable roles in modulation of addictive behaviours through personality and stress response. This study aims at exploring the relationships among personality traits, salivary cortisol and alcohol craving in alcohol-dependent subjects, and the associations between these parameters and gene polymorphisms involved. Alcohol-dependent subjects (n = 156) were recruited during a 5-day detoxification treatment. Neuroticism (N), extraversion (E) and conscientiousness (C) were measured by NEO PI-R, harm avoidance (HA), reward dependence (RD), novelty seeking (NS), persistence (P) and self-directedness (SD) were measured by Tridimensional Character Inventory. Alcohol craving level was measured by Alcohol Urge Questionnaire in the morning of day 3–day 5, and a saliva sample was collected subsequently for cortisol measurement. Genotyping was done on by PCR-RFLP. Results showed that alcohol craving correlated with salivary cortisol in female subjects (Spearman’s ρ = 0.430, P = 0.022) but not in male subjects. Alcohol craving is significantly (P < 0.05) correlated with N, C, NS and RD scores for male subjects but with E, C, NS and P scores for female subjects. Significant correlation between alcohol craving and these personality traits was only observed in DRD2 TaqIA A1-allele carriers, whose craving level was negatively correlated with RD scores (adjusted r2 = 0.191, P < 0.001). Structural equation modeling revealed the effect of DRD2 TaqIA on alcohol craving is mediated through RD trait. The current findings suggest that correlations between alcohol craving, salivary cortisol level and certain addiction-related personality traits are gender-specific. DRD2 TaqIA polymorphisms may be associated with alcohol craving level through mediation of RD trait: alcohol-dependent A1-carrying patients with more prominent RD trait may benefit from a detoxification treatment environment in which alcohol craving level is low.

P51

AUDITORY EVENT RELATED POTENTIALS (P3) AND COGNITIVE CHANGES INDUCED BY FRONTAL DIRECT CURRENT STIMULATION IN ALCOHOLICS ACCORDING TO LESCH ALCOHOLISM TYPOLOGY

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Frontal lobe dysfunction is a hallmark of alcohol dependence. Recent studies have shown that a simple but powerful technique of cortical modulation—transcranial direct current stimulation (tDCS)—can induce significant cognitive changes. We therefore aimed to assess the clinical and electrophysiological (as indexed by P3) effects of tDCS of the left dorsolateral prefrontal cortex (DLPFC) in different types of alcoholic patients according to Lesch typology. We enrolled 49 alcoholic subjects, between 18 and 75 years old, during the subacute abstinence period to participate in this study. Subjects underwent Event-Related Potential (ERP) registration of alcohol-related and neutral sounds before, during and after active tDCS (1 mA, 35 cm², during 10 min) or sham procedure in a counterbalanced and randomized order. Frontal assessment battery (FAB) and 5-items of obsessive-compulsive drinking scale were applied at the beginning and at the end of each experimental session. We found a superior improvement of FAB performance after active tDCS when compared with sham tDCS in Lesch IV alcoholics only. ERP analysis showed an increase in the mean amplitude of P3 under alcohol-related and neutral sounds, notably in the frontal site (Fz). This change was more pronounced in Lesch IV alcoholics. We showed clinical and electrophysiological evidence of tDCS-induced frontal activity enhancement that was specific for Lesch IV alcoholics. Given that frontal dysfunction may contribute to the loss of control over drinking behavior, local increase in frontal activity induced by tDCS might have a beneficial clinical impact in the future.

P52

DYNSFUNCTION OF GLUTAMERGIC PROJECTION NEURONS IN THE MEDIAL PREFRONTAL CORTEX OF RATS WITH A HISTORY OF ALCOHOL DEPENDENCE

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Understanding the pathophysiology of addictive disorders is critical for development of new treatments. A prolonged history of alcohol dependence persists, and the impact of addictive behaviour on the amygdala, recent research demonstrates a critical role for the medial prefrontal cortex (mPFC) in the inhibition of addictive behaviours. The underlying neurobiology of altered mPFC function is poorly understood. Here we induced a post-dependent state in rats using intermittent alcohol exposure. Experiments were carried out following 3 weeks of recovery to eliminate contributions of acute withdrawal. Microarray-based transcriptome analysis from mPFC, nucleus accumbens and amygdala tissue extracts followed by cluster analysis using cell-type specific gene sets (gene set enrichment analysis) pointed to mPFC projection neurons as a major site of neuroadaptations. Using laser capture microscopy-aided microdissection followed by quantitative RT–PCR, a subset of these genes (Egr2, Egr4, Nr4a1, Gm2) was found to be specifically down-regulated in highly purified infralimbic projection neurons. Furthermore, within the infralimbic region of post-dependent rats, several activity-regulated genes (Fos, Egr1, Jund) lack a response to ethanol. Finally, we found increased ethanol-evoked release of extracellular glutamate within the mPFC of post-dependent rats. Together, these data point toward profound alterations in mPFC function, in particular within the infralimbic region, and predict dysfunction of inhibitory control over behaviour in alcohol addiction. Treatments that target this region may help alleviate symptoms of addictive disorders.

P53

BIDIRECTIONAL HIPPOCAMPAL SYNAPTIC PLASTICITY IS DIFFERENTLY AFFECTED BY ETHANOL DURING BINGE DRINKING IN ADOLESCENT RATS

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Young people are particularly susceptible to the impairing effects of alcohol. Memory impairments often involve modifications in the ability of hippocampal neurons to establish long-term potentiation (LTP) and long-term depression (LTD) of excitatory neurotransmission; however, few studies have examined how repeated ethanol exposure during adolescence affects this bidirectional plasticity in hippocampus. Numerous studies have shown that cognitive deficits and alteration of LTP in hippocampus are induced by heavy drinking during adolescence. Presently, insufficient animal research has investigated the effect of EtOH exposure on the different forms of synaptic plasticity during adolescence. In the present work funded by a European INTERREG IVA grant (AlcoBinge project), we have investigated the effects of single or repeated EtOH exposure on both LTP and LTD in CA1 hippocampal neurons of adolescent Sprague-Dawley rats. Experiments were performed on dorsal hippocampal slices (400 μm thick) prepared from adolescent/peri-adolescent rats (P38-P60). Single or repeated ethanol exposure was carried out with 3.0 g/kg ethanol injected intraperitoneally in order to achieve quickly high blood ethanol concentrations. Extracellular recordings from CA1 pyramidal neurons were performed while stimuli were delivered using a bipolar stimulating electrode placed in the stratum radiatum. LTP was induced with high-frequency stimulation (3 × 100 Hz, 1 s, separated by 10 s, at test intensity) and LTD was induced after low-frequency stimulation (LFS, 1 Hz, 600 bursts). Measurements were made for 45 min following plasticity induction. Our results show that the deleterious effect of alcohol on both types of plasticity was dependent upon both the number of alcohol intoxications and the delay after being intoxicated.

P54

ALCOHOL-DEPENDENT PATIENTS WITH REPEAT ADMISSIONS

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Background. Alcohol use disorders are one of the leading causes of morbidity in Australia. The impact is wide-ranging and extensive, resulting in considerable burden on both the individual and on the healthcare system as a whole. In general hospital settings, alcohol-dependent patients account for a high proportion of all admissions and are often frequent users of inpatient services. However, despite repeated access to hospital services, patient outcomes do not appear to improve. Aims. This study aimed to retrospectively characterize patients repeatedly admitted to Royal Prince Alfred Hospital, Australia, with an alcohol-related diagnosis, and to quantify the financial cost associated with these frequent admissions.

Methods. Hospital discharge data were used to identify patients with an alcohol-related admission to Royal Prince Alfred Hospital (RPAH), Australia, on ≥3 occasions between 1 January and 31 December 2009. Three or more admissions per year to a general hospital were deemed an appropriate marker of extensive disability related to alcohol use. Information regarding patient demographics, cost weightings, specialty medical teams, diagnoses and procedures ordered was collected.

Results. A total of 1337 alcohol-related admissions to RPAH were recorded during 2009, with 74 patients admitted ≥3 times. Patients with repeat admissions were significantly older (mean age = 50 vs 42 years) and had significantly shorter stays in hospital (mean length of stay = 5 vs 7 days) than patients with discrete admissions and 77% of the repeat admissions were male. Drug and alcohol assessments were conducted in only 31% of all repeat admissions, with poor compliance (<50%) by the most common admitting teams (Emergency, Drug and Alcohol, Psychiatry and Gastroenterology). Subsequently, alcohol dependence was identified in only 51% of all admissions. The total cost to the hospital for care of the 74 patients with repeat admissions during 2009 was in excess of 1 million Australian dollars.

Conclusion. Alcohol abuse and dependence continue to be poorly identified and managed in hospital admissions. Widespread implementation of in-depth drug and alcohol assessments for all alcohol-related admissions...
could prove an invaluable tool for appropriate care formulation for and case management of chronic alcohol-dependent patients.

**P55**

**MORPHOFUNCTIONAL INDICES OF RAT BRAIN HISTAMINERGIC NEURONS IN AN HOUR AFTER SINGLE INTRAPERITONEAL INTRODUCTION OF ALCOHOL**

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The central histamine participates in regulation of various functions, systems and reactions of the organism: neuroendocrine and cardiovascular systems, brain blood flow, body temperature, sleep and awakening, feeding and drinking behavior, memory, cognition and learning. Also histaminergic system participates in a pathogenesis of many diseases, including alcoholism. The aim of this research was to estimate the alcohol influence on morphofunctional state of rat brain histaminergic neurons in an hour after single intraperitoneal introduction of 20% ethanol solution. Estimation is spent with the use of the cyto-photometric and morphometric analysis methods. In an hour after single intraperitoneal introduction of 20% ethanol solution in the dose of 4 g/kg activity of monoamine oxidase type B (MAO B), lactate DG and acetaldehyde-phosphate increase in histaminergic neurons perikarya that testifies to ascending of processes of the brain histamine oxidative deamination, additional activation of late stages of the glycolysis proceeding in anaerobic conditions, and intensifying of autophagy processes. A decrease in level G-6-ph-DG and NADPhH-DG activity is evidence of weakening extramitochondrial energy processes. In the dose of 1 g/kg, the increasing of MAO B and NADPhH-DG activity and decreasing of lactate DG activity are exposed. In an hour after single intraperitoneal introduction of 20% ethanol solution in the dose of 4 g/kg, the rat brain histaminergic neurons perikarya increase. They become more roundish and spherical. Nuclei of such cells also increase a little and approximate. In the dose of 1 g/kg rat brain, histaminergic neurons perikarya decrease in size and become more rounded. In conclusion, our data suggest that, depending on a dose, alcohol has activating or hypnotic effect on rats through histaminergic system. In a small (exciting) dose, ethanol activates brain histaminergic neurons, and in the large (narcotic) dose, it oppresses histaminergic neurons. Thereby, alcohol induces the significant structural and metabolic disturbances in brain histaminergic neurons that suggest on active participation histaminergic system in ethanol-related behaviors in rat.

**P56**

**EPGENETIC DIFFERENCES IN THE PROMOTER REGION OF THE GHRELIN RECEPTOR BETWEEN HIGH AND LOW ALCOHOL-CONSUMING RATS**

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There is growing evidence suggesting the involvement of ghrelin-signalling in the reward system. Ghrelin is an orexigenic peptide that has been shown to not only regulate food intake but also to be required for alcohol-induced reward by stimulating the ghrelin receptor, GHS-R1A, at the level of the brain. The hypothesis that ghrelin-signalling is a possible novel target for the treatment of alcohol dependence.

**P58**

**ASSESSING VIGILANCE WITH DYNAMIC PUPILLOMETRY IN PATIENTS WITH ALCOHOL DEPENDENCY**

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**Introduction.** Pupilometry is a non-invasive measurement technique based on the pupillary response to specific variables. Vigilance disturbances can be objectively measured through this automated pupil size determination. The aim of this study was to define severity of vigilance disturbances in patients with alcohol dependency according to Lesch’s typology.

**Methods.** Ninety-sixi abstinent patients (65 male, 31 female) with alcohol dependency according to ICD-10 criteria were included in a retrospective data analysis. All patients (11 inpatients, 85 outpatients) were assessed according to Lesch typology by a structured interview; further comorbidities and relevant sociodemographic data were analysed. Dynamic pupilometry was performed with a Whittacker Corpration TV Pupilometer 1050. Pupil diameters were measured every minute for a 9 min period. A decrease in pupil size correlates with an increase in vigilance disturbance.

**Results.** Twenty-five percent of the patients were classified Type I, 21.9% Type II, 39.6% Type III and finally 13.5% Type IV according to Lesch typology. The whole study population showed a decrease in pupil diameter of 9%. When analysing the four subtypes, a maximal decrease of 8.4% was found for Type I patients, 4.1% for Type II patients, 7.2% for Type III patients and finally 18.8% for Type IV patients. When compared with each other, a significant difference was found for Type IV patients, suggesting strongest disturbances in vigilance.

**Discussion.** Objectification due to dynamic pupilometry could improve validity of Lesch typology and result in improvement of therapeutic strategies. In previous studies, Lesch Type IV alcoholics showed impairments in cognitive functions. In conclusion, these results have an impact on therapeutic strategies, as vigilance is essential for psychiatric interventions.

**P60**

**ALCOHOLIC HABITS DURING PREGNANCY: AN ITALIAN STUDY IN 582 PREGNANT WOMEN**

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**Background.** Fetal alcohol spectrum disorder (FASD) is a set of developmental malformations caused by alcohol consumption during pregnancy. Fetal alcohol syndrome (FAS) is the strongest manifestation of FASD, results in short stature, microcephally and facial dysmorphogenesis including microphthalmia. One of the criteria for the diagnosis of FAS is the assessment of alcohol consumption by the mother during pregnancy. The aim of this study is to make a photo of drinking habits during pregnancy.

**Methods.** Preliminary results of this survey are underway to 582 selected pregnant women, of different nationalities, who refer at Department of Obstetrics Gynaecology Urology Science, Sapienza University of Rome. Semi-structured questionnaires were administered, assessing the unit of drinking whenever more than one drink. In the second, 35.1% consume less than one drink. Finally, in the third trimester on 37.8% of women who drink, 3.3% consume alcohol more than one drink.

**Conclusions.** Most women do not know how much drinking during pregnancy is dangerous for fetus. There is currently no cure for FAS, so there is only one sure way to prevent fetal alcohol-related conditions: completely avoid the use of alcohol during pregnancy. The consumption of alcohol during pregnancy can harm the developing fetus at all stages of pregnancy. It is therefore important to have a wide program of education. And it is essential that physicians adequately sensitize women who are pregnant or intend to start.