Methods: We performed a retrospective assessment of the prevalence of hyponatremia in 53 people receiving carbamazepine (subjects) and 64 people not receiving carbamazepine (controls) at a residential centre for the learning disabled. We examined relationships between serum sodium level, sex, age, carbamazepine dose and serum carbamazepine levels. We assessed clinical features of hyponatremia using a specially designed checklist.

Results: The prevalence of hyponatremia in subjects was 41.5% and in controls was 9.4%. Mean serum sodium level in subjects was significantly lower than that in controls ($p<0.0001$). Hyponatremia correlated significantly with high carbamazepine dose and high serum carbamazepine level. The checklist of clinical features was not useful in detecting hyponatremia clinically.

Conclusions: Hyponatremia is a common occurrence in this population. In light of the uncertain significance of mild, chronic hyponatremia, the value of routine monitoring of serum electrolytes has yet to be established.

P27.04

Risperidone for behavioral disturbances in adults

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The efficacy and safety of risperidone for treating behavioral disturbances in adults with conduct spectrum disorders and mild, moderate, or borderline mental retardation were assessed in a randomized, double-blind, placebo-controlled trial. Subjects received 1 to 4 mg/day of risperidone (n=39) or placebo (n=38) for 4 weeks. The overall mean dose of risperidone was 1.45 mg/day The primary efficacy measure was the change at endpoint in the total Aberrant Behavior Checklist (ABC) score. Significantly greater reductions in total ABC score were seen in the risperidone group than in the placebo group from week 2 through endpoint ($p<0.05$). Similar results were observed for the irritability subscale ($p<0.05$). Risperidone was associated with a significantly greater decrease than placebo in the hyperactivity and stereotypic behavior subscales at week 4 ($p<0.05$). Adverse events were reported in 59% and 66% of patients in the risperidone and placebo groups, respectively. No patient discontinued the trial because of adverse events. The results suggest that risperidone is efficacious and well tolerated for behavioral disturbances in adults with conduct spectrum disorders and subaverage IQs.

P28. Neurobiology

P28.01

Effect of naltrexone on dopamine system functions in morphine dependent rats

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Opiate receptor antagonists (ORA), including Naltrexone, are widely used in the treatment of opiate addiction. There is an opinion that the therapeutic effect of ORA is only attributed to "chemical blockade". To answer the question whether ORA have an effect on biological mechanisms of opiate dependence we studied two groups of Wistar rats. One group was given morphine for 12 days. Three days after morphine withdrawal this group received Naltrexone during 12 days. Group 2 was only given morphine. The HPLC method was used to determine free and conjugated DA in the blood serum and midbrain. The results showed an increased blood free DA level in group 2 and normal in group 1. The conjugated DA level in the blood of animals in group 2 tended to decrease while that in group 1 was normalized and DOPAC content increased thus indicating an activation of DA metabolism. In the midbrain, the morphine-increased DA level was much more increased by Naltrexone. So, Naltrexone was shown to influence DA system functions in the brain and blood of the morphine-dependent rats. This influence might be attributed to both the blockade of opiate receptors and the direct effect of Naltrexone on DA system, including DA receptors.

P28.02

Autoradiographic localisation of 5-HT receptors in the human brain

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The serotonin (5-HT) system is widely distributed throughout the brain and is a target for the pharmacological treatment of several psychiatric disorders. A detailed characterization of 5-HT receptor distribution in the human brain could be important for the development of specific psychoactive drugs. This presentation compares the distribution of a number of 5-HT receptors and the 5-HT transporter (SERT) in the human postmortem brain. Anatomically adjacent whole hemisphere sections were incubated with specific radioligands for the 5-HT1A, 5-HT1B, 5-HT2A, 5-HT4 receptors and SERT. A detailed comparison of the autoradiograms revealed different laminar and regional distribution patterns in the neocortex, where 5-HT1A and 5-HT4 receptor binding showed highest densities in superficial layers and 5-HT2A receptor binding was most prominent in medial layers. The layering was less distinct for 5-HT1B and SERT, although regional differences was revealed with dense binding in the medial occipital cortex (5-HT1B) and cingulate gyrus (SERT). Subregional differences between the different receptors were also observed in the hippocampal formation and in the basal ganglia.

P28.03

Evidence for neuroplastic activity in acute schizophrenic psychosis

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Objective: S100B, a calcium binding protein produced by astroglial cells, evolves paracrine and autocrine effects on neurons and glia cells playing a role in neuronal plasticity and long-term potentiation. It has been shown to be increased in acute brain damage and neurodegeneration. A recent study showed increased S100B levels in medicated acutely psychotic patients with schizophrenia.

Methods: The study presented here included 26 drug-free patients with acute schizophrenia and 26 matched healthy controls. S100B blood concentrations were determined using a quantitative immunoassay upon admission and after 6 weeks of neuroleptic treatment. The PANSS was used to investigate psychopathology.

Results: Unmedicated schizophrenic patients initially showed significantly increased S100B levels compared to matched healthy controls. After 6 weeks of treatment, 11 patients showed normal S100B levels while in 15 patients the levels remained increased. These patients showed significantly higher PANSS negative scores upon admission and after 6 weeks of treatment.

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Conclusions: Schizophrenic patients display ongoing neuroplastic activity in acute psychosis. Continuously increased S100B levels are associated with negative symptomatology.

P28.04

Anatomy and function of the Corpus Callosum

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This talk outlines evidence on anatomical organisation of the Corpus Callosum (CC) from ablation or radiographic studies in animals. Moreover, data of functional lateralisation as well as interhemispheric transfer in patients with agenesis or lesions of the CC are discussed: Laterality studies in these patients reveal an asymmetry in functional specialisation, i.e. left hemisphere superiority in language and right hemisphere superiority in spatial tasks. Evidence of interhemispheric transfer is reported from tests of bimanual coordination, tactile information, kinesthetic information, tactile pattern recognition in these patients. Furthermore, transcallosal inhibition (TI) of tonic voluntary hand muscle contraction or ballistic movements elicited by transcranial magnetic stimulation, is absent in patients with lesions in the trunk of the CC and suggests a role of the CC in bimanual motor coordination.

P28.05

Monaminergic systems in depressed patients with and without suicidal behavior

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Objectives: There is evidence that noradrenergic and serotonergic systems are involved in the pathophysiology of suicidal behavior. There is a lack of morphological studies on monaminergic systems in individuals with mood disorders who performed suicide (S) and those who died otherwise(NS).

Methods: In patients with mood disorders (S, NS) as compared to non-psychiatric control subjects (C), the total number of neurons and the number of serotonergic/noradrenergic neurons in the dorsal raphe and the locus coeruleus was determined in serial Nissl-stained sections and in parallel series of sections immuno-stained for tryptophan hydroxylase/tyrosine hydroxylase.

Results: In ventral parts of the dorsal raphe a deficit of Nissl stained neurons could be shown for S and NS as compared to C. In the mesencephalic part of the dorsal raphe numbers for tryptophan hydroxylase immunoreactive neurons were higher in S than in NS and C. In the locus coeruleus numbers of tyrosin hydroxylase immunoreactive neurons were higher in S than in NS, but comparable to C.

Conclusions: Results indicate a deficit of noradrenalin and serotonin synthesis in patients with mood disorders who died not by suicide. In suicides with mood disorders these deficits appear to be compensated or overcompensated. A model for suicidal behavior derived from these data will be presented.

P28.06

Gender differences in neuronal survival upon hypoxia

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17-b-Estradiol (E2) has neuroprotective properties including activation of protective pathways, antiapoptotic genes and antioxidant activities, although the distinct cellular pathways are still unknown. The biological effects of E2 are mediated via specific receptors and also receptor-independently. The aim of this study was to compare the effect of E2 on neuronal viability in female and male rat postnatal hippocampal neurons upon hypoxia (15h). Estrogen-receptors were expressed in hippocampal neurons both in vitro and in vivo. Exposure to hypoxia strongly increased cell death in male neurons, which could be dose dependently reduced by E2, whereas in female neuronal cultures the hypoxia exposure had no significant effect on cell viability. These data show for the first time a clear gender difference in neuronal vulnerability to hypoxia in vitro, independent of exogenously administered hormones. The beneficial effect of E2 on neuronal survival upon hypoxia supports the use of estrogens/selective estrogen receptor modulators as a potential neuroprotective therapy for cerebrovascular and neurodegenerative diseases.

P28.07

Endocannabinoids in schizophrenia and other psychiatric disorders

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The recent discovery of the endogenous cannabinoid system reveals new perspectives regarding the role of this system in the pathogenesis of schizophrenia. The study investigated the specific role of the endocannabinoid system in different psychiatric disorders.

Method: About 190 healthy volunteers and patients suffering either from schizophrenia, affective disorders or dementia were clinically investigated. Endogenous cannabinoids were studied in cerebrospinal fluid and plasma of these subjects and correlated to clinical symptoms.

Findings: Cerebrospinal concentrations of specific endogenous cannabinoids were significantly higher in schizophrenic patients never treated with neuroleptics than in healthy controls. These findings were specific for patients suffering from schizophrenia.

Conclusions: Endogenous cannabinoid levels in cerebrospinal fluid are specifically elevated in schizophrenic patients. This may reflect an imbalance in endogenous cannabinoid signaling, which may be a specific reaction to other neurotransmitter alterations in schizophrenia. Thus, the endogenous cannabinoid system may play an important role in the pathogenesis of schizophrenia.

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