was sampled before and 6 hours after the injection and a WBC count was made.

Results: After administrating hydrocortisone, the increase in the neutrophil count was of at least 2,000 cells/mm3 over the pre-injection value for 2 patients; for 1 patient, the increase was of 1,900 cells/mm3.

Conclusion: Testing marrow granulocyte reserve using hydrocortisone may be helpful in sorting patients with a benign neutropenia from those with an underlying blood dyscrasia. This report must be considered as a new basis for further and longitudinal research.

P47.02

Gene expression profiling of human neuronal cells treated with antipsychotics in vitro

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Clinical response and patterns of side-effects are different to treatment with "classical" (e.g. haloperidol) and novel (e.g. risperidone) antipsychotic drugs. Both show high affinity to G-protein coupled dopamine D2 receptors, which inhibit adenylyl cyclase. The further molecular mechanism of action however is not well understood yet.

This study aimed to investigate the gene regulating effects of haloperidol vs. risperidone on differentiated human neuroblastoma cells in vitro. Retinoic acid-induced differentiated SKN-SH-SY5Y cells were examined. We studied the differential gene expression profile of "treated" and "untreated" human neuronal cells after short time and long time "treatment" under different pharmacological concentrations. The differential gene expression was assessed by cDNA-microarrays containing 588 genes (ESTs). The expression of selected gene products was confirmed by RT-PCR-methods and Western blotting. Additionally the ProteinChip-technology was used for the protein expression profiling.

We identified differentially expressed genes which are involved in complex signal transduction pathways and in the dopaminergic pathway (e.g. dopamine beta-hydroxylase, MAO, COMT).

P47.03

Differential distribution of (S)- and (R)- pindolol to the rat brain

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Pindolol, a beta blocker and a partial 5-HT1A/1B agonist, accelerates and augments the clinical efficacy of antidepressant drugs. After administration of the racemates (equal parts of two mirror image forms, enantiomers) of pindolol or propranolol in rats, we have found that the concentrations of the (S)-enantiomers are higher than the (R)-enantiomers in brain but lower in plasma. The difference between (S)- and (R)- propranolol, but not (S)- and (R)- pindolol, may be explained by a difference in plasma protein binding between the two molecular conformations. In contrast to the findings in vivo, the passage of the (S)- and (R)- enantiomers of pindolol and propranolol across endothelial cells in a BBB model in vitro were not different. Contrary to expectation, verapamil (calcium channel blocker and P-glycoprotein inhibitor) seems to inhibit the influx of pindolol and propranolol into, rather than the efflux from the rat brain in vivo. These observations indicate that studies of the transport of drugs across the BBB and potential drug-drug interactions at the level of the BBB are important areas for further exploration.

P47.04

Role for the endogenous cannabinoid system in addiction

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The endogenous cannabinoid system is a new neuromodulatory system composed by several lipid transmitters (anandamide and 2-arachidonylglycerol) and G protein-coupled receptors. This system is the target of the psychoactive constituents of cannabis sativa, termed cannabinoids. The endogenous cannabinoid system has been found to be not only the neurobiological substrate of marijuana addiction, but also a relevant modulatory system of the main neurotransmitters involved in reward circuits such as dopamine, opioid peptides, GABA and glutamate. Animal models have demonstrated that drugs active at brain cannabinoid receptors are able of modulate ethanol, cannabinoid and opiate self-administration. They also modify the acquisition and expression of drug-induced conditioned place preference. Both, anandamide production and the number and efficay of cannabinoid receptors are also relevant for allostatic changes associated with drug dependence. This is reflected in the recent description of the efficacy of cannabinoid receptor antagonists as drugs capable of modify drug intake and relapse in animals with a history of dependence. All these features point to a potential role for the endogenous cannabinoid system as a new source of therapies for drug abuse.

P47.05

Apomorphine induced motility – gender and dopamine-receptor D2-genotypes

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Objectives: In male Wistar rats apomorphine (APO), a dopamine receptor (DRD) agonist, induces individually different motility patterns being differently sensitive to neuroleptics:1. sniffers (stereotyped sniffing and increased locomotor activity) 2. lickers or 3. gnawers (stereotyped licking or gnawing and differently increased locomotor activity). The stereotypies of the sniffers and gnawers are shown to be associated with different DRD2 receptor polymorphism genotypes (Germeyer et al 2001 Brain Res in press). In this study it was examined whether locomotor activation may also correlate with these DRD2 receptor polymorphism genotypes and wether gender may influence DRD-induced stereotyped or locomotor motility, too.

Methods: APO (2mg/kg s.c.)-induced motility patterns of male and female rats were recorded and observed in an Animex-Motility Meter and genotyped to their DRD2 receptor polymorphisms by direct sequencing.

Results: In APO-induced individually different stereotyped behaviour no difference between male and female rat groups was found, but in APO-induced locomotor activation, which also did not correlate with the DRD2 receptor polymorphism genotypes.

Conclusion: DRD-induced individually different locomotor activation seems to be influenced in part by gender, but not by the different DRD2 receptor polymorphism genotypes being associated with the individually different DRD2-induced stereotyped behaviour.

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