hypolocomotion was significantly attenuated by coadministration of the vanilloid receptor type 1 (VR1) antagonist capsazepine (5 mg/kg) that by itself did not affect hyperlocomotion in DAT KO mice (two-way ANOVA; $p<0.05$). We conclude that constitutive hyperdopaminergia is sufficient to produce specific and profound alterations in endocannabinoid signalling. Re-establishing endocannabinoid levels and neurotransmission alleviates hyperlocomotion in DAT KO mice and might constitute an alternative therapeutic strategy for disorders associated with hyperdopaminergia. In this process, VR1 receptors seem to play a key role and represent a novel promising pharmacological target.

P.2.156 Neonatal handling attenuates the enhancement of immobility induced by subacute phencyclidine in the forced swimming test, a schizophrenia negative symptoms-like animal model

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The period soon after birth is critical for brain development. Environmental circumstances during this period give rise to long-lasting modifications in brain plasticity. Early handling makes rats more resistant to stressful consequences and exhibit low emotional reactivity. Schizophrenia (SZ) is a neuropsychiatric disorder of unknown etiology. In humans, N-methyl-D-aspartate (NMDA) antagonists induce a psychotic state that closely resembles SZ. The enhancement of immobility in the forced swimming test (FST) induced by repeated phencyclidine (PCP), a non-competitive NMDA antagonist, has been considered as an animal model of negative symptoms of SZ, in particular avolition. Current hypotheses concerning the ethiology of SZ invoke not only neurochemical but also environmental disturbances as components to the vulnerability for this disorder. The present study investigates whether neonatal handling, which makes animals more resistant to stress, protects animals from the SZ-like symptoms induced by PCP.

Methods: Subjects were the offspring of Wistar rats, On the day of birth, all the litters were cross-fostered and culled to 10 male pups with a mother. *Neonatal handling:* Litters were randomly assigned to one of the two infantile treatment conditions: non-handled (NH) or handled (H). The H pups were removed daily from their mothers for 15 min. This procedure was repeated daily from day 1 to day 21. After weaning, the pups were then housed in groups and left undisturbed until testing on day 60. *Phencyclidine administration:* Two months old animals received subacute treatment with either saline (S) or PCP (5 mg/kg/day) in one of the following combinations: H+S, H+PCP, NH+S and NH+PCP for 5 consecutive days. *Forced Swimming test:* After PCP administration, the animals were tested in a glass tank according to Porsolt et al., 1979. Briefly, on the first day, rats were gently placed in the water for a 15-min period of habituation. The next day, they were once more placed in the glass tank and observed for 5 min. The behaviour of the animals was videotaped and analysed manually. The duration of immobility (floating and making only those movements necessary to keep the nose above the water) was recorded.

Results: a) neonatal handling, by itself, led to a significant reduction in the immobilisation time as compared to NH animals; b) PCP administration in NH animals prolonged the immobilisation time compared with S treatment; c) PCP failed to enhance immobilization in H animals.

Immobilisation time (s) in the forced swimming test induced by PCP in H and NH rats.

H	H-PCP	NH	NH-PCP
55.5±13.3[a]	94.2±13.7[b,c]	131.0±12.0[d]	179.3±18.8

[a] $p<0.0007$ vs NH; [b] $p<0.05$ vs NH; [c] $p<0.002$ vs NH-PCP; [d] $p<0.04$ vs NH-PCP.

Conclusions: Neonatal handling attenuates the enhancement of immobility induced by repeated PCP in the FST. This effect could be due to the improved behavioural adaptation to the environment, including enhanced adaptive response to stress, produced by handling in infancy. The dopaminergic innervations might be involved since PCP exposure led to a selective reduction in basal and stress-evoked dopamine utilization, and DA appears to be a critical neuromodulatory influence in stress responses.

References

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P.2.157 Decreased platelet serotonin transporter in patients with psychotic disorders

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Introduction: Different findings support the role of the serotonin (5-HT) system in the pathophysiology of some psychotic symptoms and in the mode of action of atypical neuroleptics. In the present study, we aimed to measure the platelet 5-HT transporter, similar to that present in the brain, through the specific binding of [^{3}H]paroxetine, a selective compound for labelling it, in platelets of out- and inpatients affected by psychotic disorder, as compared with healthy controls. The presence of possible correlations between biological and psychopathological features was examined as well.

Patients and Methods: Fifteen patients (7 women and 8 men, mean age±SD: 32±8 years), who met DSM-IV-R criteria for bipolar disorder (mixed state), schizophrenia or schizoaffective disorder, were included in the study. Fifteen healthy drug-free subjects (7 women and 8 men, mean age±SD: 30±8 years) were included as control subjects, and were completely drug-free.

Venous blood (25 ml) was collected from fasting subjects, between the hours of 8 to 9 a.m. and during the months of February to March. Platelet membranes and the [^{3}H]paroxetine binding were carried out according to standardized methods. The protein concentration was measured according to the method of Peterson [13]. Equilibrium-saturation binding data, the maximum binding capacity (B_{max}, fmol/mg) and the dissociation constant (K_d, nM) were analysed by means of iterative curve-fitting computer programmes EBDA [14].

Results: The binding was specific and saturable and the Scatchard analysis revealed the presence of one population of high-affinity binding sites. The B_{max} and K_d values of the patients were, respectively, 853±140 and 0.11±0.05, those of the control subjects were, respectively, 1368±172 and 0.09±003. The B_{max} was significantly lower in the patients than in the