effects of antidepressant therapy. Here, we investigated whether chronic antidepressant treatment of rats induced changes of the mitochondrial number in hippocampus.

Methods: For this report, the effects of the tricyclic antidepressant imipramine were tested in two strains of rats; the Sprague – Dawley and the other strain from the Flinders sensitive line, which has been bred to a phenotype with certain ''depressive-like'' phenotype. Design-based stereological methods were used to estimate the number and the volume of mitochondria of mitochondria in CA1 stratum radiatum (CA1SR) of the hippocampus.

Results: The results showed that the number of mitochondria in CA1SR was significantly smaller in the FSL saline group compared to the FRL saline group. However, the mean volume of mitochondria was significantly larger in the FSL saline group compared to the FRL saline group. Following treatment, the FSL imipramine group showed a significant increase in the number of mitochondria compared to the FSL saline group. But treatment with imipramine did not induce significant differences in the number of CA1 mitochondria between the SD saline group and SD imipramine group.

Conclusion: In conclusion, our results support the mitochondria plasticity hypothesis that depressive disorders and the pharmacological treatment thereof may be related to impairments of mitochondria plasticity in the hippocampus and that antidepressant treatment may counteract the structural impairments.

P-15-006 βCCT as well as flumazenil prevent the diazepam withdrawal-induced anxiety in the elevated plus maze in rats

J. Divljakovic[1], T. Timic[1], M. Milinkovic[1], B. Batinic[1], M. Van Linn[2], J. Cook[2], M. Savic[1]. [1]*Faculty of Pharmacy, Belgrade, Serbia;* [2]*University of Wisconsin, Milwaukee, USA*

Objective: Despite a half century of clinical use and the recognized potential of benzodiazepine dependence, the mechanisms underlying benzodiazepine withdrawal remain insufficiently understood. The aim of the present study was to assess the influence of the non-selective antagonist (flumazenil) and the preferential α1-subunit selective antagonist (βCCt) on the anxiety level after diazepam withdrawal.

Methods: The male Wistar rats were protractedly treated during 21 days with diazepam (2 mg/kg) or solvent. On the testing day, 24 hours after the last injection, animals from the diazepam-treated groups received either antagonist (flumazenil or βCCt) or solvent, and animals from the solvent-treated groups received solvent or diazepam. Twenty minutes after administration of treatment on the testing day, single animals were placed in the elevated plus maze in order to assess the level of anxiety.

Results: Two-way ANOVA revealed that animals withdrawn from diazepam spent significantly less time on the open arms than control animals ($p=0.023$). One-way ANOVA, followed by post hoc test, revealed that administration of flumazenil (10 mg/kg) or βCCt (1.25, 5 or 20 mg/kg) reversed the diazepam withdrawal-induced anxiety (percentage of open arm time: $p=0.003$, $p=0.032$, $p=0.031$ and $p=0.014$ compared to the diazepam-withdrawn group, respectively). Concomitant administration of antagonists (10 mg/kg flumazenil, or 1.25, 5 or 20 mg/kg βCCt) induced an anxiolytic effect comparable to that observed after acutely administrated diazepam (percentage of open arm time: $p=0.142$, $p=0.187$, $p=0.243$ and $p=0.290$, respectively).

Conclusion: The present study demonstrated that administration of the α1-selective antagonist βCCt or non-selective antagonist flumazenil could prevent the withdrawal-induced anxiety and also induce an anxiolytic-like effect. Moreover, presented results have suggested that mechanism of preventing the withdrawal-induced anxiety involves the antagonism at α1-containing GABAA receptors.

P-15-007 Effects of novel dopaminergic derivates on depression-like behavior: A pilot study

J. Fedotova. *Institute of Physiology, RASci, St. Petersburg, Russia*

Objective: Recent evidences suggest that the dysfunction of the central dopaminergic pathways may be a critical component of the neurobiological basis of depression. The effects of novel dopaminergic substances, 3,4-dimethoxyphenylethylamine derivates, on experimental model of depression were studied in male rats after acute or chronic administration in comparison to those of the classical antidepressant, clomipramine.

Methods: The novel DA derivates, PK-2111, PK-2122, PK-2123, PK-2126 (0,1, 1,0, 10,0 mg/kg, i.p.) and clomipramine (50.0 mg/kg) were injected acutely (1 h prior to behavioral testing) or chronically (for 21 days, the last injection being made 1 h prior to behavioral testing) in animals subjected to the forced swimming test (FST) and the locomotor activity test.

Results: In dose of 0.1 mg/kg PK-2122 exerted depressant-like effect, while in doses of 1.0 or 10.0 mg/kg PK-2122 exerted antidepressant-like effect as compared with the control group. Chronic treatment with PK-2123 or PK-2122 (0.1, 1.0 or 10.0 mg/kg) produced antidepressant-like effect which was significant as compared with control group and group treated with clomipramine. Also, chronic treatment of PK-2122 in high dose of 10.0 mg/kg induces antidepressant-like effect as compared with the control group, and this effect was less effective than it in a doses of 0.1 and 1.0 mg/kg.

Conclusion: These results suggest that PK-2126 independently from dose and PK-2122 in the middle and high doses may be effective in experimental model of depression in rats when administered acutely, PK-2111, PK-2122 or PK-2123 may be effective in experimental model of depression in rats when administered repeatedly.

P-15-008 The role of the 5-HT1A receptor in the murine 5-HT-syndrome

H. Fink[1], R. Haberzettl[1], B. Bert[1], J. Brosda[1]. [1]*Inst. PharmTox, Berlin, Germany*

Objective: In humans the incidence of the serotonin (5-HT)-syndrome has increased over the last decade, likely due to a higher prescription rate of serotonergic drugs. The 5-HT-syndrome can be evoked by serotonergic drugs in high doses. It is characterized by severe autonomic, neuromuscular and mental symptoms. It is also possible to elicit a 5-HT-syndrome in mice, which has been linked to the occurrence of the Straub tail response. We revealed in male NMRI mice five core responses that reliably occur and dose-dependently increase in frequency and intensity after the treatment with fluoxetine, 5-HTP, and tranylcypromine as well as their combinations. Here, we investigated which signs of the 5-HT-syndrome are mediated by the 5-HT1A-receptor.

Methods: We administered a full 5-HT1A-receptor agonist, 8-OH-DPAT, and a partial 5-HT1A-receptor agonist, buspirone, in increasing doses to male NMRI mice and assessed the occurrence and intensity of 15 behavioral and physiological responses including body temperature.

Results: Both agonists produced all five core responses (hindlimb abduction, low body posture, tremor, piloerection, decrease of rearing). Exclusively the 8-OH-DPAT induced the Straub tail, which was not evoked by buspirone and any other tested serotonergic agonist.

Conclusion: 5-HT1A-receptor activation elicits the core responses of the murine 5-HT-syndrome. However, the Straub tail response was only provoked by the full agonist. Based on the presynaptic 5-HT1A-receptor reserve and the higher intrinsic activity of the full agonist, the Straub tail response seems to be associated to postsynaptic 5-HT1A-receptor activation. Therefore, the Straub tail response is not a parameter for describing the 5-HT-syndrome in mice.

P-15-009 Different contributions of nucleus accumbens subregions to probabilistic reversal learning

S. Floresco[1], G. Dalton[1], C. Eades[1], A. Phillips[1]. [1]*University of British Columbia, Vancouver, Canada*

Objective: Impairments in positive reinforcement mechanisms and behavioural flexibility are core features of clinical depression. Cognitive deficits associated with depression have been demonstrated using a probabilistic decision-making task. Disruption in nucleus accumbens (NAc) functioning has been linked to motivational and cognitive abnormalities associated with the disorder. Studies in animals have revealed dissociable roles for NAc subregions in different aspects of behavioural flexibility. Interestingly, lesions in these brain regions do not impair flexible responding on simpler (ie: non-probabilistic) reversals. However, contribution to more complex