NMMA receptor subunits were determined in some brain regions of mice exposed to the stress.

**Results:** Acute and repeated administration of desipramine, sertraline, and aripiprazole did not attenuate deficits of social behaviors in mice exposed to stress as juveniles. Co-administration of aripiprazole with sertraline repeatedly and administration of memantine acutely showed a tendency and significant, respectively, to attenuate deficits of social behaviors. Utilization of serotonin/dopamine and the phosphorylated protein levels of NR2A were decreased and increased, respectively, in some brain regions of mice showing deficits of social behaviors.

**Conclusion:** These findings suggest that social defeat stress as juveniles induces the development of antidepressant-treatment-resistant deficits of social behaviors related to monoaminergic and/or glutamatergic dysfunction. Serotonergic and dopaminergic activators or glutamatergic inhibitors may be a strategy for treating to attenuate the treatment-resistant deficits.

**PS135**

**Effects of the mineralocorticoid receptor antagonist spironolactone in a treatment-resistant model of depression in female rats**

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**Abstract**

In recent studies we have shown that the tryptophan (TRP) depletion model of depression previously validated in male rats is paroxetine-resistant in females (Franklin et al. 2015). In this model, we found that secretion of the mineralocorticoid hormone aldosterone increased after 4 days of TRP depletion and surprisingly prior to corticosterone enhancement. The study aim was to investigate the effects of mineralocorticoid receptor (MR) blockade on depression-like behaviour induced by TRP depletion.

Female rats were fed a control (0.2% of TRP) or low TRP diet (0.04% of TRP) for 14 days. They were simultaneously treated with the MR antagonist spironolactone (1.2 mg/rat/day) or placebo via matrix-driven delivery pellets (Innovative Research of America, USA) for 14 days. Rats were tested in the Forced Swim Test (FST) on treatment day 14. Animals were sacrificed by decapitation on day 15.

Two-way ANOVA showed that TRP depletion resulted in an increased immobility time in the FST. Further analysis showed that TRP-depleted rats treated with spironolactone but with placebo spent a significantly shorter time immobile compared to controls. Rats exposed to TRP depletion exhibited significantly higher serum concentrations of aldosterone and corticosterone, which were slightly modified by spironolactone treatment. TRP depletion significantly enhanced serum interleukin-6 as well as gene expression of orexin A, a neuropeptide related to ghrelin, which has been shown to be altered in patients with treatment-resistant depression.

Findings show that treatment of rats with the MR antagonist spironolactone results in a mild improvement of TRP depletion-induced depression-like behaviour. Blockade of aldosterone action could represent a target for new antidepressant treatment.

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**PS136**

**Time-dependent alteration of reward-induced dopamine release in the nucleus accumbens of the neuropathic pain model rats.**

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**Abstract**

Chronic pain is frequently comorbid with psychiatric disorders such as depression, suggesting the common neuroplastic changes in the central nervous system. It has been considered that chronic pain lowers the function of mesolimbic reward circuits and leads to depression-like states. Nucleus accumbens (NAC) is one of the key structures of the mesolimbic dopaminergic system, which is well known to play an important role in the reward circuits. Extracellular dopamine (DA) levels in the NAC elevate after the acquisition or prediction of rewards. In this study, we examined the reward-induced DA release in the NAC of neuropathic pain model rats. To prepare the neuropathic pain model, the spinal nerve was ligated (SNL model), and reward-induced DA release in the NAC was examined in 4 weeks after SNL surgery. The animals were given with two types of rewards, 30% sucrose solution or pain relief by intrahemical injection of pregabaline (100 μg/10 μl PBS), and DA release was monitored using an in vivo microdialysis technique. Both rewards increased extracellular DA levels in the NAC 2 weeks after SNL surgery. In contrast, neither sucrose solution nor pain relief increased the DA release 4 weeks after SNL surgery. These results suggest that dysfunction of the mesolimbic reward circuits occurred 4 weeks, but not 2 weeks, after SNL surgery.

**PS137**

**Evidence that Cannabidiol Induces Acute Antidepressant-Like Effects in Different Animal Models**

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**Abstract**

**Objectives:** Cannabidiol (CBD), a non-psychotomimetic compound of Cannabis sativa, induced antidepressant-like effects in rodents tested in the forced swimming and olfactory bulbectomy models (Zanelati et al., 2010, Linge et al., Neuropharmacology, 2015). However, no study so far has investigated CBD effects in animal models with greater construct validity for depression, such as the learned helplessness and the Flinders Sensitive and Flinders Resistant Line (FSL/FRL). The present work aimed at investigating the acute effects of CBD in these models.

**Methods and Results:** Experiment 1. For the learned helplessness (LH) paradigm male Wistar rats were submitted to the pre-test (inescapable footshocks) and test (escapable shocks) sessions with a seven days interval. A single injection of CBD (10, 30 mg/Kg, ip), imipramine (15 mg/Kg, ip) or vehicle was given to rats either after pre-test or 1h before test. Another group received daily injections of imipramine (15 mg/Kg/day, ip), between the pre-test and test, as a positive control for the antidepressant effect.