hyperlocomotion. Hydrolysis inhibition of anandamide and 2-AG didn't inhibited cocaine-action. However when combined with a subthreshold dose of rimonabant, hydrolysis inhibition of 2-AG attenuated cocaine-hyperlocomotion. None of the compounds induced changes in basal locomotion. Finally we test if this interaction between cannabinoid receptors in conditioned place preference (CPP) protocol. As expected Rimonabanto(10 mg/kg) innibited the acquisition of cocaine-induced CPP. Confirming our hypothesis the CB2-R antagonist reversed this rimonabanto-effect.

Conclusion: Our results demonstrate that CB1-R blockade and CB2-R activation interact to prevent cocaine-induced hyperlocomotion. We also showed that 2-AG has a important role in this process. In conclusion we proposed that blockade of CB1 receptor redirects 2Ag action to CB2 receptor, and the activation of this last is responsible by prevent cocaine-response. This represents a possible mechanism through which the endocannabinoid system modulates the effects of this psychostimulant drug.

P.1.g.049 Chronic etanercept treatment exerts antidepressant-like effect in cafeteria diet-fed rats

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Purpose of the study: An increasing number of studies have revealed that obesity is associated with depression. Recent studies also have reported that obesity is not only as a metabolic disorder but also as an inflammatory disease. Moreover, it has been suggested that proinflammatory cytokines cause depressive symptoms and anti-TNF-α treatment ameliorated these symptoms of patients. We have previously demonstrated that TNF-α inhibition decreased depression-like behaviour in an animal model of depression [1]. The purpose of the present study was to investigate the effect of chronic etanercept, a TNF-α inhibitor, on depressive-like behavior in cafeteria diet (CD)-fed rats.

Methods: Male weanling Wistar Albino rats (50–70 g, 30 days after birth) were divided into three groups (n = 10): First group of rats (control) was fed on standard pelleted diet. The second group of animals (obese) was fed on CD which is a high-fat diet in order to generate a diet-induced obesity model as reported previously [2]. This diet was composed by a mixture of pate, bacon, chips, cookies, chocolate and chow with proportions of 2:1:1:1:1:1, respectively, and was given to each rat daily. The last group (etanercept-treated) was also fed on CD and treated with etanercept (0.8 mg/kg/weekly/subcutaneously) during 12 weeks. The body weights of animals were measured weekly. Forced swimming test (FST), the sucrose consumption and preference test were used to investigate antidepressant effect of etanercept. Total locomotor activity (TLA) was also measured. Significant differences were determined using one-way ANOVA followed by Tukey's post hoc tests. The level of significance was assumed to be $p < 0.05$.

Results: After 12 weeks, the body weight of obese group was higher than control ($p < 0.0001$) and etanercept-treated group was lower than both control and obese group ($p < 0.0001$). There was no significant difference between three groups in terms of TLA ($p > 0.05$). In FST, there were differences between three groups in terms of immobility time during second day of testing ($F(2,27) = 12.09$, $p = 0.0002$). Obese rats exhibited more immobility than control group ($p < 0.001$), while there was no difference between control and etanercept-treated group ($p > 0.05$). Sucrose consumption in obese group was significantly lower than the control group ($p < 0.05$). However, there was no significant difference between etanercept-treated and control group in terms of sucrose consumption ($p > 0.05$). In sucrose preference test, the obese group preferred sucrose less than control group ($p < 0.0001$) and the behavior of rats in etanercept-treated group did not differ significantly from the control group ($p > 0.05$).

Conclusions: The results of present study indicated that chronic etanercept treatment decreased depressive-like behavior in CD-fed rats, indicating that TNF-α may play a crucial role in obesity-related depression. The data strongly suggest that etanercept may be useful in clinical practice as an antidepressant drug moreover its co-administration with antidepressant drugs may potentiate their clinical efficacy in patients.

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P.1.g.052 Serotonin transporter-independent actions of the antidepressant vortioxetine as revealed in studies of the SERT Met172 mouse

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Purpose: Depression is one of the most common and burdensome disorders worldwide. The most widely prescribed antidepressants are serotonin (5-HT) selective reuptake inhibitors (SSRIs), believed to provide therapeutic benefit by inhibiting 5-HT reuptake by the 5-HT transporter (SERT) and thus elevating extracellular 5-HT levels. To improve efficacy, a number of drugs have been developed that offer additional target engagements, including other neurotransmitter transporters and receptors. The efficacy of such agents raises important questions as the degree to which one (e.g., SERT) or more of the anticipated targets accounts for therapeutic efficacy. Even for SSRIs, statements as to target requirements rely on data from the small fraction of assayable targets expressed by the mammalian genome.

Methods: In the present report, we describe our efforts to investigate antidepressant targeting specificity using a novel transgenic mouse model in which the high-affinity interactions of many antidepressants at the SERT has been disabled without alteration of 5-HT transport function. In this effort, we seek to understand the degree to which vortioxetine, an approved antidepressant, requires SERT antagonism in acute tests with predictive validity for antidepressant efficacy given that the drug also has significant interactions with 5-HT1A, 5-HT1B, 5-HT1D, 5-HT3 and 5-HT7 receptors at clinically relevant doses.

Results: Using the SERT M172 mouse model [1], we provide evidence that the acute, antidepressant actions of vortioxetine do not require SERT antagonism. In initial studies, using 5-HT uptake assays in human SERT M172 transfected cells and SERT M172