inhibits serotonin reuptake. Compared to S-(+)-ketamine, the less potent anesthetic enantiomer R(-)-ketamine requires much more additional concentration effect studies for its analgesic and antidepressant effects.

PS129

Low TNFAIP3 was normalized with antidepressant in patients with major depressive disorder

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Abstract

Rationale: Abnormalities in Toll-like receptors (TLRs) expression in depression have been inferred in part from observed increases in TLR4 levels in peripheral blood mononuclear cells (PBMCs) and postmortem brains of depressed and suicidal patients. Activation of the TLR4 pathway partially explained the inflammatory status in patients with major depressive disorder. However, the negative regulators for TLR4 pathway have never been investigated.

Objectives: *In vivo*, the mRNA expression levels of negative regulation genes including SOCS1, TOLLIP, SIGIRR, MyD88, NOD2, and TNFAIP3 in PBMCs were examined in 56 patients with MDD and 35 health controls. The mRNA expression levels were assessed in parallel with a housekeeping gene using qRT-PCR before and after treatment with antidepressants. We also investigated the *in vitro* effects of fluoxetine on the TNFAIP3 expression. First, TNFAIP3 in human monocytes (THP-1 cell line) was measured by qRT-PCR after treated with fluoxetine (10^{-8}-10^{-5} M). Second, we pretreated monocytes, which had TNFAIP3 gene knockdown, with fluoxetine before LPS-stimulation. Then, interleukin 6 (IL-6) and tumor necrotic factor alpha (TNFα) were measured by qRT-PCR.

Results: *In vivo*, TOLLIP, MyD88, NOD2 and TNFAIP3 were expressed at lower levels in patients with MDD. Only TNFAIP3 was significantly increased and normalized by treatment with antidepressants for 4 weeks. *In vitro*, fluoxetine could significantly increase TNFAIP3 mRNA expression in human monocyte. The suppressive effects of fluoxetine on IL-6 and TNFα decreased partially after knockdowning TNFAIP3 gene.

Conclusions: These findings suggest that antidepressant treatment exerts anti-inflammatory effects in patients with MDD partially through increasing expression of TNFAIP3 gene. Further studies investigating the effects of manipulating TNFAIP3 gene on depression is needed to fully elucidate the underlying mechanism.

Keywords: negative regulation, toll-like receptor, innate immunity, major depressive disorder, inflammation

PS130

Maternal fluoxetine treatment influences anxiety- and depressive-like behaviours in adolescent offspring: a rodent model

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Abstract

Objective: Approximately 10% of pregnant women are prescribed antidepressant drugs, most commonly the selective serotonin reuptake inhibitor, Fluoxetine. Fluoxetine crosses the placenta and is excreted in breast milk raising concerns regarding the consequences of infant exposure. The aim of this study was to evaluate the effects of maternal Fluoxetine treatment on offspring behaviours of relevance to neurodevelopmental and psychiatric disorders, using a rodent model of depression.

Methods: Sprague-Dawley (SD; healthy model) and Wistar-Kyoto (WKY; depression model) pregnant rats were treated with Fluoxetine (10mg/kg/day) or vehicle, from gestational day 0 to postnatal day 14 (~5 weeks in total). Once offspring reached adolescence (~5 weeks of age), locomotor activity, anxiety-like and depressive-like behaviours were assessed using the open field test (OFT), elevated plus maze (EPM) and forced swim test (FST).

Results: Fluoxetine exposed offspring displayed an increase in distance travelled in the OFT, an effect that was independent of rat strain and sex. Fluoxetine exposure also caused an increase (up to 50%) in time spent in the corners of the OFT in SD male and WKY female rats compared to their respective vehicle controls. Similarly, in the EPM, maternal Fluoxetine treatment resulted in a significant increase in time spent in the closed arms in SD males and WKY males (29–52%). A similar trend was observed in females, but this did not reach significance. In the FST, maternal Fluoxetine treatment increased immobility time in exposed offspring (28%), an effect that was independent of strain or sex.

Conclusion: Maternal Fluoxetine treatment resulted in significant increases in anxiety-like and depressive-like behaviours in exposed offspring, largely independent of the rat model used. However, further studies in various models of maternal depression are required to confirm these preliminary findings and establish the effects of Fluoxetine exposure on the developing brain.

PS131

Transcriptomic evidence for dematuration of the mouse frontal cortex and hippocampus by chronic antidepressant treatment

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Abstract

The selective serotonin reuptake inhibitor, fluoxetine (FLX), is widely used to treat depression and anxiety disorders, but mechanisms underlying its antidepressant effect remain largely unknown. Previous studies that evaluated several molecular and/or electrophysiological features of the maturation stages of each neuron type have demonstrated that FLX treatment can reverse the established maturation of certain types of neurons in the hippocampus and frontal cortex (FC). However, this dematuration effect of FLX in the adult brain has not been assessed with regard to genome-wide gene expression patterns.

In this study, we compared gene expression patterns in the FLX-treated FC and hippocampus of adult mice with those of the corresponding brain regions of normal infant mice. The gene expression patterns of FLX-treated mice significantly resembled those of normal infant mice in the FC and, to a large extent, in the hippocampus. In addition, time-course analyses of the ages of infant mice used in the comparisons with FLX-treated mice indicated that the gene expression patterns of FLX-treated mice were most similar to those of the youngest infants examined (1-week-old hippocampus and 2-week-old FC).