S01-02 - **FASTER AND SAFER ANTIDEPRESSANT-LIKE RESPONSE INDUCED BY PHARMACOLOGICAL BLOCKADE OF 5-HT$_7$ RECEPTORS**

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**Objectives:** In term of efficacy and onset of action, current antidepressant drugs still suffer from important drawbacks. Hence, we recently assessed whether the pharmacological blockade of serotonin 7 receptors [5-hydroxytryptamine (5-HT7) receptors] can produce a faster and safer antidepressant response than fluoxetine (Prozac®), the most prescribed antidepressant.

**Methods and results:** In rats, we showed that SB-269970, a selective 5-HT7 receptor antagonist, exerts an effective antidepressant-like effect as assessed in the forced swim test. Moreover, we revealed *in vivo* that 5-HT7 receptors negatively regulate the firing activity of dorsal raphe 5-HT neurons and become desensitised after a chronic treatment with fluoxetine. In contrast to fluoxetine, a one-week treatment with SB-269970 did not decrease 5-HT neuronal firing activity but desensitized 5-HT autoreceptors, enhanced the hippocampal cellular proliferation rate and counteracted the anxious/depressive-like behaviour that present the olfactory bulbectomized rat model. Finally, early life treatment with fluoxetine, but not with SB-269970, induced anxious/depressive-like behaviours in adulthood.

**Conclusions:** These results indicated that the 5-HT7 receptor participates in both mood regulation and the antidepressant effect of SSRIs, and that 5-HT7 receptor antagonists may represent a new class of antidepressant drugs with safer and faster therapeutic action.

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