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INVOLVEMENT OF THE LATERAL SEPTAL NUCLEUS AND $GABA_A$ RECEPTORS IN THE ANTIDEPRESSANT-LIKE EFFECTS OF ALLOPREGNANOLONE IN WISTAR RATS

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Introduction: Pharmacological and non-pharmacological antidepressant therapies increase the firing rate of lateral septal nucleus neurons (a brain structure involved in mood state regulation) and reduce immobility in the forced swim test (FST), whereas the neurosteroid allopregnanolone appears to produce antidepressant-like effects through actions at $GABA_A$ receptors.

Objective: To explore the participation of the lateral septal nucleus and $GABA_A$ receptors in the antidepressant-like effects of allopregnanolone in Wistar rats.

Methods: First, the minimally effective dose of allopregnanolone that produces antidepressant-like effects in the FST was determined. Second, the effect of this minimally effective dose in the FST was evaluated on the firing rate of lateral septal neurons. Third, the antidepressant-like effects of microinjection of allopregnanolone (1.0 µg/rat) into the lateral septal nucleus was evaluated in the FST. Fourth, we explored whether the effects of allopregnanolone on the lateral septal neuron firing rate and FST are blocked by picrotoxin or bicuculline, two $GABA_A$ receptor antagonists.

Results: The minimally effective dose of allopregnanolone with antidepressant-like effects in the FST was 1.0 mg/kg (i.p.) and significantly increased the firing rate of lateral septal neurons. Microinjection of allopregnanolone into the lateral septal nucleus produced antidepressant-like effects in the FST. Pretreatment with picrotoxin and bicuculline blocked the increase in lateral septal neuron firing rate and the antidepressant-like effects of allopregnanolone in the FST.

Conclusion: The lateral septal nucleus participates in the antidepressant-like effects of allopregnanolone through actions on $GABA_A$ receptors in Wistar rats.

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