EFFECT OF REPEATED TREATMENT WITH MIRTAZAPINE ON THE CENTRAL DOPAMINERGIC D$_2$/D$_3$ RECEPTORS

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Mirtazapine (MIR) is an antidepressant drug which enhances noradrenergic and serotonergic 5-HT$_{1A}$ neurotransmission via antagonistic action at central α$_2$-adrenergic autoreceptors and heteroreceptors. We reported earlier that tricyclic antidepressants administered repeatedly induced adaptive changes in the central dopaminergic D$_2$/D$_3$ receptors. Therefore, we designed our present study to determine whether repeated MIR treatment could evoke similar effect. The experiments were carried out on male Wistar rats. MIR was administered at a dose of 10 mg/kg once or repeatedly (twice daily for 14 days). The obtained results showed that MIR administered repeatedly potentiated the hyperlocomotion induced by D-amphetamine but not by quinpirole or 7-OH-DPAT. Biochemical study showed that MIR administered repeatedly decreased the binding of $[^3]$Hquinpirole (a D$_2$/D$_3$ receptor agonist) in the shell part of the nucleus accumbens septi and in the islands of Calleja but did not change the binding in the nucleus caudatus (medial or lateral). On the other hand, both acute and repeated drug treatment did not change the $[^3]$H7-OH-DPAT (a D$_3$ receptor agonist) binding sites in the islands of Calleja as well as in the shell part of nucleus accumbens septi. In addition, MIR did not alter the level of mRNA encoding dopamine D$_2$ receptors, not only after repeated but also after acute treatment. The above results indicate that repeated MIR administration did not induce any adaptive change (behavioral and biochemical changes) in the dopaminergic D$_2$/D$_3$ system.

**Key words:** mirtazapine, repeated treatment, dopamine D$_2$/D$_3$ receptors, adaptive changes, rats