Modafinil Improves Catalepsy in a Rat 6-Hydroxydopamine Model of Parkinson's Disease; Possible Involvement of Dopaminergic Neurotransmission

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Abstract

Purpose: Modafinil is a vigilance-enhancing drug licensed for narcolepsy. The use of modafinil leads to various neuromodulatory effects with very low abuse potential. A body of evidence suggested that modafinil may have anti-parkinsonian effects. This study was designed to evaluate whether modafinil could improve motor dysfunction in the 6-hydroxydopamine (6-OHDA)-induced rat model of Parkinson's disease.

Methods: Male Wistar rats (180-220 g, n= 98) were used in this study. Parkinsonism was induced by injection of 6-hydroxydopamine (10 mu g/2 mu l in 0.2 % ascorbic acid-saline) into the right striatum. Parkinsonian rats received intraperitoneal (ip) injections of modafinil (50, 75, and 100 mg/kg) and catalepsy-like immobility was assessed by the bar test (BT). Furthermore, involvement of dopamine D-1 and D-2 receptors in modafinil's anti-parkinsonian effects was studied. For this purpose, parkinsonian animals were pretreated with SCH23390 and raclopride (the dopamine D-1 and D-2 receptor anatgonists, respectively) or SCH23390 + raclopride, and then assessed by the BT.

Results: Modafinil (100 mg/kg) showed anti-cataleptic effects in the BT. Notably, the effect of modafinil in the BT was reversed in parkinsonian rats pretreated with raclopride (1.25 mg/kg) and/or SCH23390 + raclopride (0.75 and 1.25 mg/kg, respectively), but not in those pretreated with SCH23390 (0.75 mg/kg).

Conclusion: Acute administration of modafinil improves 6-OHDA-induced motor impairment possibly through activation of dopamine D-2 receptors.

Keywords

Author Keywords: 6-hydroxydopamine; Dopaminergic neurotransmission; Modafinil; Parkinson's disease; Rat

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