



Repeated administration of the dopaminergic agonist apomorphine: development of apomorphine aggressiveness and changes in the interaction between dopamine D₂ receptors and G-proteins

Ruth Rudissaar¹, Jaanus Harro², Katrin Pruus¹, Ago Rincken³,
Lembit Allikmets¹

¹Department of Pharmacology, University of Tartu, Ravila 19, 50411, Tartu, Estonia

²Department of Psychology, Center of Behavioral and Health Sciences, University of Tartu, Tiigi 78, 50410, Tartu, Estonia

³Institute of Organic and Bioorganic Chemistry, University of Tartu, Jakobi 2, 51014, Tartu, Estonia

Correspondence: Katrin Pruus, e-mail: katrin.pruus@ut.ee

Abstract:

The repeated administration of dopamine receptor agonists produces a progressive increase in the acute behavioral effects of these drugs, known as behavioral sensitization. These includes the development of impulsive aggressive behavior after repeated small doses of apomorphine. The aim of this investigation was to study the behavioral specificity of the apomorphine-induced aggressiveness model and its possible relationship with changes in the D₂ receptor-G-protein interaction. Apomorphine (1 mg/kg, *sc*) was administered daily for three weeks to two groups of male Wistar rats. One of the groups was repeatedly tested for the development of aggressiveness. Apomorphine aggressiveness developed stepwise with repeated behavioral testing. Neither apomorphine-treated group displayed any behavioral change in the open field test, forced swimming test, or quipazine-induced wet-dog shake response test. Three weeks of apomorphine administration in the home cage increased the GDP binding affinity and reduced the [³⁵S]GTPγS binding in striatal membranes, but this effect was not present in apomorphine-treated rats that had developed aggressiveness. In conclusion, sensitization to apomorphine, as measured by the expression of aggressiveness, developed only with accumulating apomorphine-induced fighting, was behaviorally specific, and appeared to be dependent on the D₂ receptor-G-protein interaction. The absence of sensitization to the dopaminergic stimulation may be mediated by the downregulation of D₂ receptor sensitivity *via* changes in the GDP affinity of G-proteins.

Key words:

apomorphine-induced aggressiveness, quipazine-induced wet-dog shakes, forced swimming test, open field test, [³⁵S]GTPγS binding
