Effect of cocaine sensitization on $\alpha_1$-adrenoceptors in brain regions of the rat: an autoradiographic analysis

Irena Nalepa¹, Tadeusz Witarski¹, Marta Kowalska¹, Małgorzata Filip², Jerzy Vetulani¹

¹ Department of Biochemistry, ² Department of Pharmacology, Institute of Pharmacology, Polish Academy of Sciences, Smętna 12, PL 31-545 Kraków, Poland

Correspondence: Irena Nalepa, e-mail: fnalepa@cyf.krz.edu.pl

Abstract:
We investigated the effects of repeated intermittent cocaine treatment, resulting in behavioral sensitization, on the density of $\alpha_1$-adrenoceptors in the rat brain measured by quantitative in vitro autoradiography of $[^3H]$prazosin. Animals were decapitated following a short (2 h) and long (48 h) withdrawal period after an injection of cocaine (10 mg/kg) on day 10 given to either cocaine-naive (saline daily, days 1–5) or cocaine-sensitized (cocaine 10 mg/kg daily, days 1–5) rats. In cocaine-naive rats, significant decreases in $\alpha_1$-adrenoceptors 2 h after a single dose of cocaine were observed in the amygdaloid nuclei and hippocampus; the decreases in the centromedial nucleus of the amygdala persisted until 48th hour of withdrawal. On the contrary, increases in $\alpha_1$-adrenoceptors after 2-h withdrawal were seen in the nucleus accumbens core and retrosplenial cortex. In cocaine-sensitized rats, the density of $\alpha_1$-adrenoceptors 2 h after a single dose of cocaine were observed in the amygdaloid nuclei and hippocampus; the decreases in the centromedial nucleus of the amygdala persisted until 48th hour of withdrawal. On the contrary, increases in $\alpha_1$-adrenoceptors after 2-h withdrawal were seen in the nucleus accumbens core and retrosplenial cortex. In cocaine-sensitized rats, the density of $\alpha_1$-adrenoceptors 2 h after the challenge with cocaine increased in the centrolateral amygdala, while in the granular retrosplenial cortex and in the most of thalamic nuclei, the densities of $\alpha_1$-adrenoceptors decreased. After 48-h withdrawal, the density of $\alpha_1$-adrenoceptors increased in the nucleus accumbens core and shell (by 21% and 58%, respectively), and in the amygdaloid centromedial and basolateral nuclei (by ca. 24%), while the decline was still observed in some thalamic nuclei. Our study shows for the first time that cocaine sensitization produces significant (dependent on the withdrawal time) alterations in the $\alpha_1$-adrenoceptor density, and the changes in some parts of the thalamus seem to be related to processes of cocaine relapses.

Key words: $[^3H]$prazosin binding, $\alpha_1$-adrenergic receptor, rat, brain structure, cocaine sensitization; autoradiography