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Effects of the noradrenergic neurotoxin DSP-4 on the expression of α_1-adrenoceptor subtypes after antidepressant treatment

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Abstract:
We have previously reported that chronic imipramine and electroconvulsive treatments increase the α_{1A}-adrenoceptor (but not the α_{1B} subtype) mRNA level and the receptor density in the rat cerebral cortex. Furthermore, we have also shown that chronic treatment with citalopram does not affect the expression of either the α_{1A}- or the α_{1B}-adrenoceptor, indicating that the previously observed up-regulation of α_{1A}-adrenoceptor may depend on the noradrenergic component of the pharmacological mechanism of action of these antidepressants. Here, we report that previous noradrenergic depletion with DSP-4 (50 mg/kg) (a neurotoxin selective for the noradrenergic nerve terminals) significantly attenuated the increase of α_{1A}-adrenoceptor mRNA induced by a 14-day treatment with imipramine (IMI, 20 mg/kg, *ip*) and abolished the effect of electroconvulsive shock (ECS, 150 mA, 0.5 s) in the prefrontal cortex of the rat brain. The changes in the receptor protein expression (as reflected by its density) that were induced by IMI and ECS treatments were differently modulated by DSP-4 lesioning, and only the ECS-induced increase in α_{1A}-adrenoceptor level was abolished. This study provides further evidence corroborating our initial hypothesis that the noradrenergic component of the action of antidepressant agents plays an essential role in the modulation of α_{1A}-adrenoceptor in the rat cerebral cortex.

Key words:
α_{1A}-adrenoceptor, DSP-4, electroconvulsive shock, HPLC, imipramine, mRNA, northern blot, [^{3}H]prazosin binding