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Short communication

Neonatal co-lesion by DSP-4 and 5,7-DHT produces adulthood behavioral sensitization to dopamine D_2 receptor agonists*

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Abstract:
To assess the possible modulatory effects of noradrenergic and serotoninergic neurons on dopaminergic neuronal activity, the noradrenergic and serotoninergic neurotoxins DSP-4 N-(2-chlorethyl)-N-ethyl-2-bromobenzylamine (50.0 mg/kg, *sc*) and 5,7-dihydroxytryptamine (5,7-DHT) (37.5 μg *icv*, half in each lateral ventricle), respectively, were administered to Wistar rats on the first and third days of postnatal ontogeny, and dopamine (DA) agonist-induced behaviors were assessed in adulthood. At eight weeks, using an HPLC/ED technique, DSP-4 treatment was associated with a reduction in NE content of the corpus striatum (> 60%), hippocampus (95%), and frontal cortex (> 85%), while 5,7-DHT was associated with an 80–90% serotonin reduction in the same brain regions. DA content was unaltered in the striatum and the cortex. In the group lesioned with both DSP-4 and 5,7-DHT, quinpirole-induced (DA D_2 agonist) yawning, 7-hydroxy-DPAT-induced (DA D_3 agonist) yawning, and apomorphine-induced (non-selective DA agonist) stereotypies were enhanced. However, SKF 38393-induced (DA D_1 agonist) oral activity was reduced in the DSP-4 + 5,7-DHT group. These findings demonstrate that DA D_2- and D_3-agonist-induced behaviors are enhanced while DA D_1-agonist-induced behaviors are suppressed in adult rats in which brain noradrenergic and serotoninergic innervation of the brain has largely been destroyed. This study indicates that noradrenergic and serotoninergic neurons have a great impact on the development of DA receptor reactivity (sensitivity).

Key words:
DSP-4, 5,7-DHT, biogenic amines, brain, dopaminergic, behavior, rats

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