

EXPRESSION OF DOPAMINE D2 AND D3 RECEPTORS AND ACTIONS OF DOPAMINERGICS ON SPINAL CIRCUITS IN WILDTYPE AND D3 KNOCKOUT MICE

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Little is known on the role of dopamine (DA) in modulating spinal cord function, or its contribution to dysfunction after injury or in neurodegenerative diseases. The hypothalamic A11 region is the sole source of spinal DA with projections to both autonomic and somatic motor regions, however, the physiological relevance of A11 and its projections are unknown. Using Sprague-Dawley rats, Wildtype (WT), and functional D3 receptor knockout (Drd 3^{-/-} KO) mice, we initiated studies to determine how DA and D2/3 receptor agonists modulate local circuits in the spinal cord.

In situ hybridization and immunolabeling showed that both D2 and D3 receptor subtypes were expressed stronger in the ventral horn of WT mice than in the functional KO mice.

Pharmacological studies of reflex responses were undertaken in the lumbar cord regions. Dorsal roots or peripheral nerves were stimulated in the isolated spinal cord. In rat and WT mice, application of DA (1-10 μ M) decreased the reflex amplitude by 20%, but had no effect in KO mice. During washout, a rebound or a facilitation of the reflex amplitude was observed. In contrast, Pergolide (Permax[®]), a D3-receptor agonist used to treat Restless Legs Syndrome (RLS) generally slightly enhanced the reflex amplitude in WT and KO mice, while the D2/D3 receptor agonists quinpirole and bromocriptine generally decreased the amplitude in both mice strains.

We conclude that DA inhibitory actions in Drd 3^{-/-} KO mice are impaired likely due to loss of D3-receptor function and reduced D2-receptor expression. This reduction of DA control over spinal reflex excitability in the somatic regions of KO mice is consistent with behavioral observations of increased motor activity (Ondo et al., 2000).

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