# Differential regulation of dopamine D1 receptor signaling in subregions of the striatum

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Recent studies demonstrated that corticostriatal projections and a histochemically defined organization of the striatum are different among subregions of the striatum. Therefore, we investigated dopamine signaling in each subregion of the striatum. Mouse striatal slices were divided into seven subregions: (1) rostral part, (2-1) intermediate medial part, (2-2) intermediate lateral part, (2-3) intermediate most lateral part, (3) caudal part, (4) most caudal part, (5) nucleus accumbens. Slices of seven subregions were treated with a D1 receptor agonist, SKF81297, and the activity of cAMP/PKA signaling was evaluated with the phosphorylation of DARPP-32 and GluA1. The effects of SKF81297 on the phosphorylation were the lowest in the subregion (3) in the rostrocaudal axis and in the subregion (2-3) in the mediolateral axis. Treatment of slices with a PDE10A inhibitor, papaverine, or SKF81297 plus a muscarinic receptor antagonist, atropine or MT3, increased the phosphorylation in subregions where the effects of SKF81297 was low. In a 6-OHDA parkinsonism model, the 6-OHDA lesion of dopaminergic innervation enhanced dopamine D1 signaling in most of subregions except subregion (3). Thus, differential regulation of dopamine D1 signaling in subregions of the striatum are mediated through activities of PDE10 and/or muscarinic receptors. Moreover, in the 6-OHDA parkinsonism model, dopamine D1 signaling is upregulated in subregions with high and low dopamine D1 signaling.