IJAE Vol. 115, n. 1/2 (Supplement), 2010

Chemical anatomy of intrastriatal tyrosine hydroxylase-neurons in neonatal life

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Dopamine (DA) axons in the developing striatum cluster in discrete areas called "DA islands". During the third postnatal week, most DA islands are no-longer detectable and the DA innervation becomes uniform. In this study we explored the relationship between the pattern of DA innervation and the number of striatal tyrosine hydroxylase (TH) positive cells during early postnatal development. By using dedicated stereology we found that the newborn striatum contains striatal TH cells, which cluster around newly sprouted DA axons. The number of these cells decreases when DA axons develop a full pattern of striatal innervation. This condition suggests a causal relationship between the amount of striatal DA innervation and the presence of striatal DA neurons. A better knowledge of the mechanisms regulating the ontogenesis of the nigrostriatal DA system may pave the way to strategies of neurorescue of the DA system

The biological role of these cells is unknown but they could represent a striatal storage of DA under condition of DA depletion. Striatal TH cells in neonatal striatum decrease during development. We treated mice with the inhibitor of the enzyme TH, alpha-methyl-*p*-tyrosine (150 mg/kg, i.p., every 24 hours from PN4 to PN8). This treatment increased the number of TH-positive intrastriatal cells. To examine the role of DA receptors in the modulation of striatal TH positive cells, we treated mice every 24 hours from PN4 to PN8 with a D1 receptor partial agonist or selective D1 receptor antagonist, SCH23390 (0.1 mg/kg, i.p.), the selective D2/3/4 receptor agonist Quinpirole (1 mg/Kg, i.p.) or the selective D2/D3 receptor antagonist, raclopride (0,1 mg/kg, i.p.). We found a significant increase of the number of the intrastriatal TH-positive cells at PN8 in animals subjected to pharmacological blockade of D1 or subjected to pharmacological activation of D2/D3 receptors. These data characterize for the first time DA cell bodies in the striatum and demonstrate their DA-dependency while showing the selective modulation upon activation of different DA receptors.

Key words
Neurogenesis; dopamine neurons; dopamine islands