

Targeting Trends

Reporting the latest news in Molecular Surgery

A specific immunotoxin elucidates a causal role of striatal cholinergic system in behavioral flexibility

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Behavioral flexibility is broadly defined as the ability to change behavioral strategy, according to a change of governing rules. Accumulated evidence suggests the involvement of particular brain areas such as prefrontal cortex and striatum in this function, in which specific brain regions play their own roles. An extension of understanding on neural substrates mediating behavioral flexibility needs a next step beyond the specificity of brain regions: the specific role of different neuronal subtypes. A method utilizing specific neurotoxins enabled us to target and elucidate the role of neurochemically-specific neurons in this ability. In our recent study,¹ we demonstrated a causal role of rat cholinergic interneurons in the striatum in behavioral flexibility, using a new specific immunotoxin targeting neurons containing choline acetyltransferase (ChAT). Comparing non-selective neuronal labeling and specific immunostaining of ChAT neurons indicated that local injections of the immunotoxin successfully and selectively damaged cholinergic neurons (Fig. 1). This result is consistent with a previous study that used Anti-ChAT-SAP to study the medial prefrontal cortex (Cat. #IT-42).²

Using the selective lesion, we compared intact rats injected with saline and rats without cholinergic interneurons of either dorsomedial or ventral striatum in a set-shifting task.³ This task required animals to shift their attention from one stimulus dimension to

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Denise Higgins, Editor

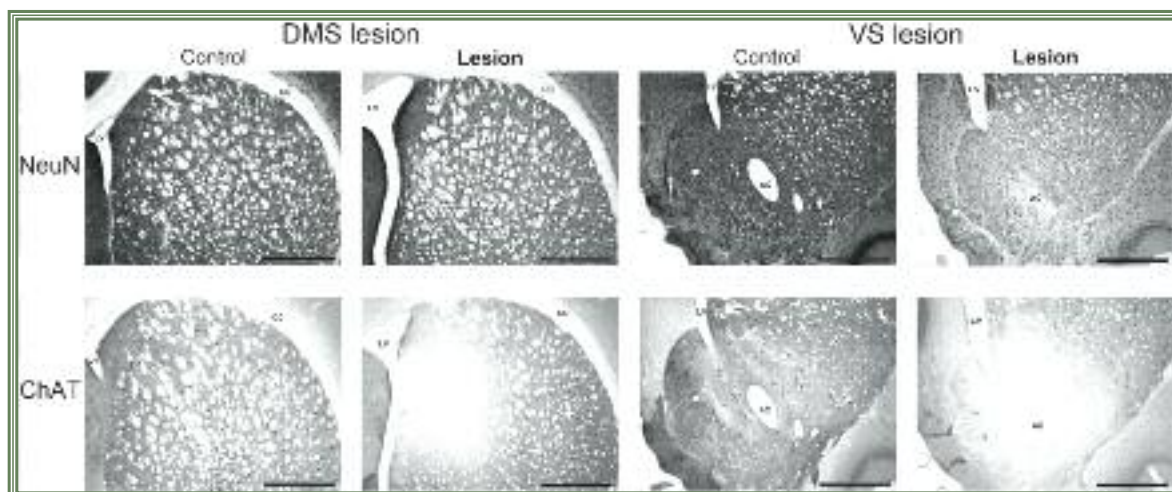


Fig. 1: Representative coronal sections of the rat striatum show intact nuclei (NeuN) staining but clear ablation of the cholinergic interneurons with ChAT staining in lesioned cases (DMS or VS). Abbreviations: DMS: dorsomedial striatum, VS: ventral striatum, LV: lateral ventricle, CC: corpus callosum, AC, anterior commissure. Scale bar: 1 mm. Reprinted from Aoki *et al.* (2015).

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