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Targeting Trends

Reporting the latest news in Molecular Surgery

Role of medial septal GABAergic neurons in learning and extinction: Effects of the novel GABA immunotoxin GAT1-SAP

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The medial septum and diagonal band of Broca (MSDB) provide a major afferent pathway to the hippocampus.[1] Cholinergic and GABAergic neurons are the main components of this pathway, but glutamatergic and peptidergic neurons also contribute.[1-5] Damage of MSDB neurons or the septohippocampal pathway impairs learning and memory, and disrupts hippocampal theta rhythm.[6-7] Although the role of cholinergic septal neurons in learning and memory and hippocampal function is well studied, little is known about the contribution of noncholinergic neuronal populations. In previous studies, intraseptal kainic acid was found to preferentially damage noncholinergic MSDB neurons, to drastically reduce hippocampal theta rhythm, and to impair spatial reversal learning.[8-11] The current study was performed to assess the cytotoxic and behavioral effects of a novel GABAergic toxin.

GAT1-SAP is a rabbit antibody to the GABA transporter GAT1 that is conjugated to the ribosome-inactivating protein, saporin. The behavioral effect of GAT1-SAP administration into the MSDB was assessed in two versions of the water maze and in an active avoidance task. In one version of the water maze, the escape platform remained in the same location every day (reference memory). In the second version, the escape platform was moved to a new location every day (working memory). For this study, rats

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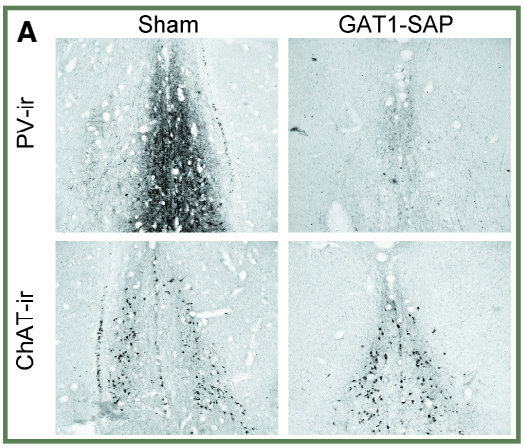

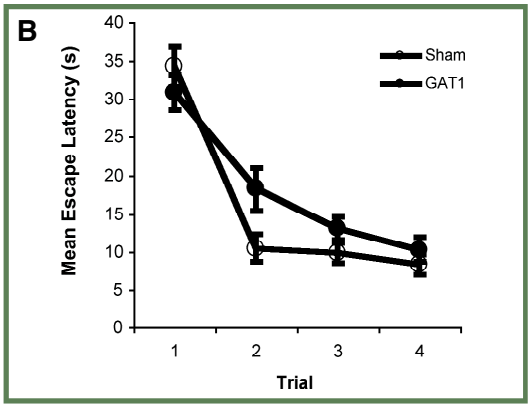

Figure 1.
A. Photomicrographs of the medial septum following a sham (left) or GAT1-SAP (right) lesion. Intraseptal GAT1-SAP reduced the number of GABAergic septohippocampal neurons, as demonstrated by parvalbumin-immunoreactivity (top). In contrast, GAT1-SAP did not remarkably affect the number of cholinergic cells, as visualized by choline acetyltransferase-immunoreactivity (bottom).
B. Within session learning was impaired in the working memory version of the water maze following GAT1-SAP treatment.

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Denise Higgins, Editor

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