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Targeting Trends

Reporting the latest news in Molecular Surgery

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Denise Higgins, Editor

ADVANCED TARGETING SYSTEMS

Effects of Intraseptal Orexin-Saporin on Spatial Memory

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Hypocretin (or orexin) neurons are located in the hypothalamus and have been implicated in various functions including sleep, arousal and feeding. One area receiving dense hypocretin projections and expressing hypocretin-2 receptors (H-2r) is the medial septum (MS), an area important in learning and memory. In the medial septum, hypocretin-2 receptors are located on cholinergic and GABAergic projection neurons that innervate the hippocampus and other limbic structures. Previous studies demonstrated that activation of H-2r excites both populations of MS neurons. Our studies investigated whether MS neurons that receive hypocretin innervation are important for spatial memory (Smith and Pang, 2005).

Male Long Evans rats were administered orexin-saporin (orexin-SAP, Cat. #IT-20) into the MS (0.6 µl) and diagonal band of Broca (DB; 0.4 µl into each DB) at three concentrations: 100, 200 and 300 ng/µl. Following a 2-week recovery period, rats were trained on a water maze task. Each daily session consisted of 6 trials. After behavioral testing, brain sections were stained to visualize cholinergic and GABAergic septohippocampal (SH) neurons using immunocytochemistry for choline acetyltransferase (ChAT) and parvalbumin (PV), respectively.

The damage caused by orexin-SAP is shown in Figure 1. Orexin-SAP at 100 ng/µl primarily damaged GABAergic SH neurons, sparing most cholinergic SH neurons. The concentration of 200 ng/µl caused more neuronal damage. At this concentration, a more substantial loss of cholinergic neurons was observed, but GABAergic neurons again showed more damage than cholinergic neurons.

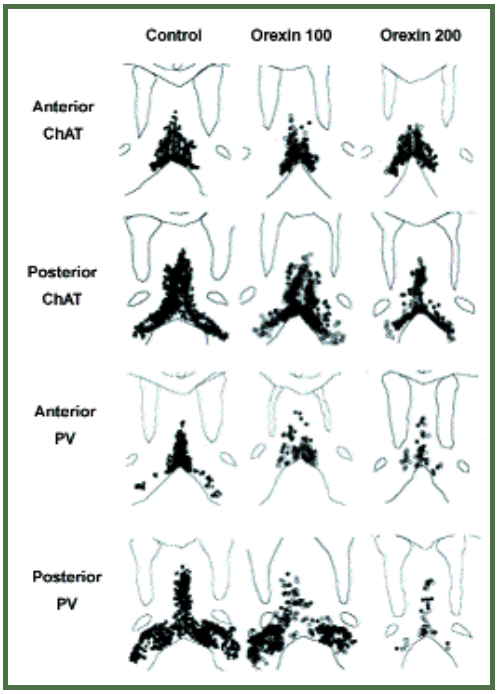

Figure 1. Cholinergic and GABAergic projection neurons in the MSDB region of control rats, and rats treated with 100 ng/µl, or 200 ng/µl of orexin-SAP. The distribution of neurons (closed squares) is drawn for a representative example of the control group. For rats treated with orexin-SAP, open circles represent the distribution of neurons from the rat with the least amount of damage, and the closed circles represent neurons from the rat with the most amount of damage in each treatment group. Originally published in Smith & Pang, 2005.

Finally, the highest concentration of orexin-SAP (300 ng/µl) produced extensive damage to the medial septum, causing shrinkage and non-specific damage of the MS-DB tissue and enlargement of the ventricles. Because of the non-specific tissue damage produced by administration

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