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Targeting Trends

Reporting the latest news in Molecular Surgery

Deletion of Catecholaminergic Neurons by Anti-DBH-Saporin Disrupts Hypothalamic MAP Kinase and CREB Activation

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The brain has evolved adaptive mechanisms for coping with stress and responds to stressors in highly stereotyped ways. One of the major physiological responses to stressful stimuli, the secretion of pituitary and adrenal hormones, is controlled by corticotropin-releasing hormone (CRH)-expressing neurons located in the paraventricular nucleus of the hypothalamus (PVH). CRH neuroendocrine neurons constitute the primary control center in the brain for initiating hormonal responses to stress, and the control of these neurons by other parts of the brain has been the subject of intensive investigation. One of the most massive sources of input to these neurons is the collection of axonal inputs originating from subpopulations of catecholaminergic (CA) neurons located in the hindbrain. These CA neurons are critical regulators of the mammalian stress axis,

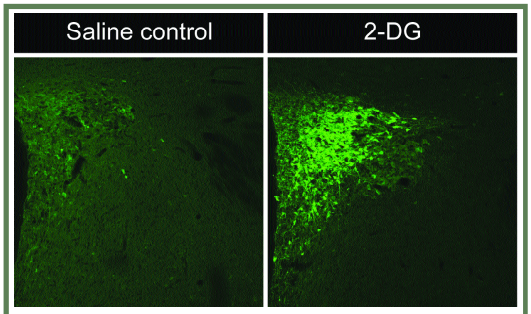

Figure 1. Levels of phospho-ERK1/2 (green signal) are elevated in the PVH in animals receiving intravenous 2-DG, as compared to saline-injected control animals.

releasing the neurotransmitters epinephrine, norepinephrine and other co-localized peptide hormones (such as neuropeptide Y) onto CRH neuroendocrine neurons.

A key question about this input system concerns its role in carrying information to the CRH neuroendocrine system to mediate responses to various stressors. We have previously shown that glycemic challenges such as 2-deoxyglucose (2-DG) or insulin, both of which produce changes in glucose concentrations when injected intravenously, trigger activation of CRH neuroendocrine neurons and are also associated with increases in the plasma concentrations of stress hormones[1,2]. The activation of

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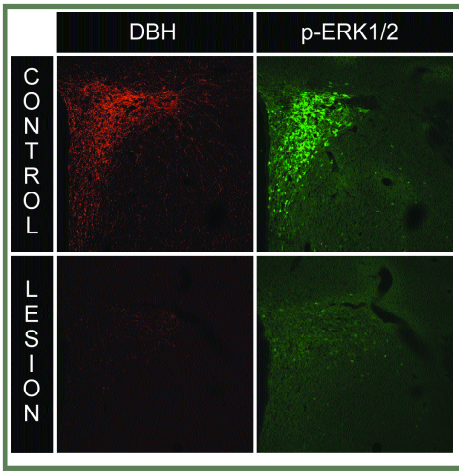

Fig 2. Rats receiving PVH injections of anti-DBH-SAP show a marked loss of catecholaminergic inputs, as seen from the drastic reductions in DBH immuno-staining (red signal, left column). This loss was accompanied by a loss of insulin-induced phospho-ERK1/2 signaling (green signal, right column).

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Denise Higgins, Editor

ADVANCED TARGETING SYSTEMS