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Targeting Trends

Reporting the latest news in Molecular Surgery

Selective lesions of amygdala intercalated neurons using the Dermorphin-SAP immunotoxin reveal their role in extinction of conditioned fear.

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Introduction by Douglas Lappi, Ph.D., President/CSO:

This quarter's Cover Article is from Ekaterina Likhtik who reprises her recently published work in Nature *454:642-645. In the News and Views, Sah and Westbrook comment that "Neuronal receptors in these circuits—such as those targeted with saporin in Likhtik and colleagues' study—are likely to become targets for the development of specific treatments for many anxiety disorders."*

The amygdala is a key subcortical structure in the neural circuit that processes acquisition as well as extinction of conditioned fear. Although a large body of literature details how amygdala activity results in fear conditioning, fear extinction circuits are less well understood. In particular, it is difficult to study the role that one of its potentially important cell groups, the intercalated (ITC) cells, may play in this behavior. These cells likely constitute an important interface between the input and output nuclei of the amygdala, gating information flow out of the amygdala during fear conditioning and extinction.[1,2]

To date the obstacle to studying the ITC cells is that they occur in small, anatomically distributed clusters[3] and are therefore difficult to selectively lesion using conventional methods. In order to circumvent this issue, we took advantage of the high levels of μ-opioid receptor expression observed in ITC cells in the light microscope. Indeed, a more detailed analysis using electron microscopy, revealed that the ITC cells express μ-opioid receptors post-synaptically at 3-6 times the rate of surrounding amygdala nuclei (Fig

(continued on page 6)

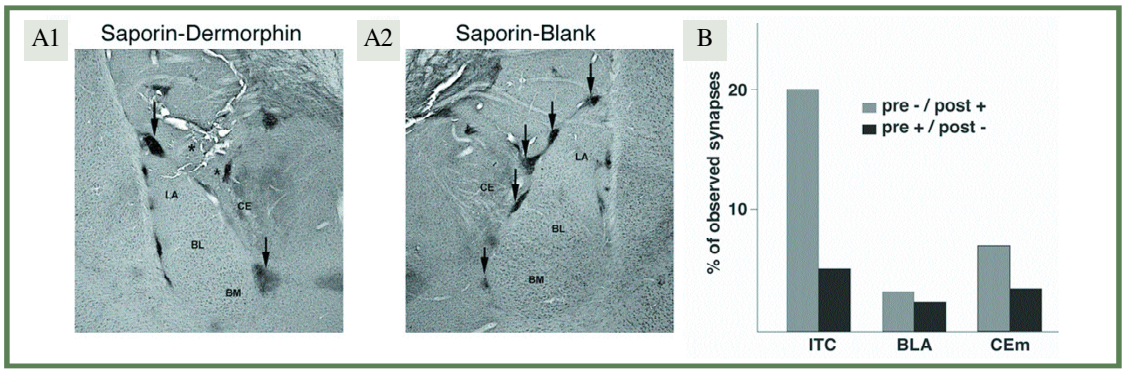

Figure 1. Dermorphin-SAP infusions lead to a spatially circumscribed loss of μ-opioid receptor immunoreactivity. **(A)** Coronal sections from rats that received either Dermorphin-SAP (A1) or Blank-SAP **(A2)** injections in the vicinity of ITC cells. Arrows indicate the remaining ITC cell clusters in the two animals. Asterisks point to injection tracks. Note that only cell clusters adjacent to tracks are affected by the infusion. **(B)** Electron microscopy: proportion of synapses where μ-opioid receptor immunoreactivity was found in post-synaptic (grey) or pre-synaptic (black) elements of the basolateral (BLA), medial central (CEm) or ITC nuclei.

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