IGF-1 modulates neuronal function | Science Signaling

Sci. Signal. 22 Mar 2016:
Vol. 9, Issue 420, pp. ec64
DOI: 10.1126/scisignal.aaf7074

Sensory experiences change neural circuits by altering the strength, number, or type of connections between neurons in the circuit. Mardinly *et al*. analyzed changes in gene expression in vasoactive intestinal peptide (VIP)–positive neurons of the mouse visual cortex. One of the transcripts enriched in VIP-positive neurons after light exposure was that encoding insulin-like growth factor 1 (IGF-1). Although knocking out *Igf1* specifically in these neurons had no effect on the gross morphology of the cortex or the size of the neurons, electrophysiological experiments indicated that these neurons received reduced inhibitory synaptic input. Knocking out *Igf1* in VIP-positive neurons reduced inhibitory inputs onto these neurons in a cell-autonomous manner, but did not affect inhibitory input onto other types of neurons in the cortex. The isoform of *Igf1* expressed in VIP-positive neurons included a heparin-binding domain, which may reduce diffusion of the secreted protein, thus limiting its range of action. Overexpressing *Igf1* in VIP-positive neurons increased inhibitory synaptic inputs onto these neurons. Electrophysiological experiments using *Igf1*-knockout and *Igf1*-overexpressing VIP-positive neurons revealed that IGF-1 acted on presynaptic neurons to increase the number or strength of inhibitory synapses onto VIP-positive neurons. Mice in which *Igf1* was knocked down in VIP-positive neurons had increased visual acuity compared to controls. However, this enhanced visual acuity disappeared when the mice were deprived of light. Thus, IGF-1 produced by VIP-positive neurons alters visual circuits in a manner that is dependent upon sensory experience. IGF-1 also alters the sensitivity of peripheral neurons. In work previously published in *Science Signaling*, Zhang *et al*. found that IGF-1–mediated signaling increased the sensitivity of peripheral neurons to painful stimuli by promoting the activation of voltage-gated T-type Ca^{2+} (Ca_V3) channels, which increased the excitability of these neurons. These studies show that IGF-1 modulates more than just neurogenesis and neural metabolism—it affects neuronal function by modulating excitability and synaptic connections.

A. R. Mardinly, I. Spiegel, A. Patrizi, E. Centofante, J. E. Bazinet, C. P. Tzeng, C. Mandel-Brehm, D. A. Harmin, H. Adesnik, M. Fagiolini, M. E. Greenberg, Sensory experience regulates cortical inhibition by inducing IGF1 in VIP neurons. *Nature* **531**, 371–375 (2016). [PubMed]

Y. Zhang, W. Qin, Z. Qian, X. Liu, H. Wang, S. Gong, Y.-G. Sun, T. P. Snutch, X. Jiang, J. Tao, Peripheral pain is enhanced by insulin-like growth factor 1 through a G protein–mediated stimulation of T-type calcium channels. *Sci. Signal*. **7**, ra94 (2014). [Abstract]