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A real turn-off

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The *Drosophila* hormone allatostatin reversibly inactivates mammalian neurons expressing its receptor.

Too many voices talking at once can make it impossible to hear what is said. Similarly, it is difficult to determine the actions of one group of neurons while hundreds more are at work. Tan *et al*. report a technique to reversibly silence groups of neurons in a recent article in *Neuron*.

Allatostatin is a peptide hormone in insects that inhibits the synthesis of juvenile hormone. In mammalian cells, allatostatin acts at allatostatin receptors to open G-protein-coupled inward-rectifying potassium channels, resulting in reduced membrane potential and input resistance.

The authors inserted allatostatin receptors into an adenoviral vector containing a neuron-specific promoter. They then injected transgene-expressing adenovirus into the rat barrel cortex, which receives sensory input from the whiskers. Thirty-five days later, they stimulated the whisker pads of anesthetized rats and recorded local field potentials (LFPs) from the barrel cortex. Within minutes of application to the exposed cortical surface, allatostatin reduced LFP response to 28%, and saline washout returned LFP response to greater than 100% of untreated levels. The authors could repeatedly inactivate and reactivate the same neurons. After the experiment, they confirmed that the recordings were done in regions that expressed the transgene. The technique worked equally well in ferret visual cortex, in which allatostatin reduced the mean firing rate of allatostatin receptor-expressing neurons to 3% of untreated levels.

Allatostatin also inactivated allatostatin receptor-expressing neurons below the surface of the brain. The authors showed visual stimuli to anesthetized ferrets during single- and multi-channel recordings from neurons in the lateral geniculate nucleus (LGN) of the thalamus. Allatostatin and saline were delivered through separate channels of micropipettes positioned near the LGN. Allatostatin injection caused a larger reduction in cellular activity than did saline. However, complete inactivation required a second allatostatin injection because of cerebrospinal fluid reflux into the micropipette, according to the authors. Saline washout was not possible in the thalamus, and the inactivation of LGN neurons lasted approximately 60 minutes.

Primate LGN neurons expressing allatostatin receptors required more allatostatin to inactivate, but remained silent longer relative to similar neurons in the ferret. Three injections of allatostatin were required to completely silence LGN neurons in the monkey. The neurons inactivated within 10 minutes of the final allatostatin injection and did not recover during the duration of the experiment. The authors also used allatostatin to inhibit neurons in transgenic mice with conditional expression of allatostatin

receptors.

Allatostatin induced nearly complete inactivation in allatostatin receptor-expressing neurons specifically and repeatedly, without any desensitization. In addition to offering the ability to 'knock out' the contributions of brain nuclei and structures, the authors believe this technique will allow the functional differentiation of seemingly similar populations of cortical neurons.

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1. Tan, E. M. *et al.* Selective and quickly reversible inactivation of mammalian neurons in vivo using the *Drosophila* allatostatin receptor. *Neuron* **51**, 157–170 (2006). | Article |