Gonadotropin-inhibiting hormone (GnIH) regulates spontaneous action potentials in anorexigenic proopiomelanocortin neurons and orexigenic neuropeptide Y cells

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Energy homeostasis and reproduction are intimately related and the mechanisms for such a close connection are the subject of considerable attention. However, our understanding of the neurobiological basis for this phenomenon is still incomplete. Neuropeptide Y (NPY) is a potent orexigen that is produced by cells in the arcuate nucleus of the hypothalamus. In the same nucleus, cells express the proopiomelanocortin (POMC) gene that produces melanocortins which are anorectic. Gonadotropin-inhibiting hormone (GnIH) peptide is a recently discovered inhibitory regulator of reproduction that is released by neurons localized in the dorsomedial nucleus of the hypothalamus, which is a nucleus with a role in regulating appetite and energy balance. It has been reported that central injections of GnIH increase food intake in birds and rats. Since GnIH neurons provide input to subsets of NPY and POMC cells, the aim of this study was to determine the effects of GnIH on the electrical activity of these appetite regulating neurons of the arcuate nucleus.

We used mice in which NPY or POMC genes were tagged with a transgene for renilla and green fluorescent protein. Mice were killed, the brain was rapidly removed into an ice slurry, and 250 μm thick coronal slices were cut. Slices were mounted in a recording chamber on the platform of an upright microscope and continuously superfused with artificial cerebrospinal fluid (aCSF) at 32°C. GFP-expressing cells were identified using epifluorescence, and patch electrodes were positioned using infrared DIC optics. Patch-clamp recordings of spontaneous action potential activity were made in whole-cell current-clamp mode or in cell-attached mode.

GnIH inhibited the firing rate of POMC cells. Since these cells are anorexigenic this inhibition may be involved in the increase of food intake induced by GnIH. The GnIH regulation of NPY cells was more complex. In one group of NPY cells, GnIH inhibited spontaneous action potential activity and this effect was associated with a clear hyperpolarisation of the membrane potential. Another group of NPY cells showed no effect of GnIH. The combined presence of blockers of glutamatergic and GABAergic receptors decreased spontaneous action potential activity. Under these conditions, GnIH evoked an increase in action potential activity.

In conclusion, these data indicate that GnIH, in addition to having an important role in regulating reproductive function, is also a significant regulator of the appetite/energy expenditure system within the hypothalamus.