

Hypothalamic arcuate nucleus: neurons in the meeting-point of central autonomic and neuroendocrine regulatory systems

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The arcuate nucleus, an elongated group of cells in the medio-basal hypothalamus occupy a key position in neuroendocrine and autonomic regulatory mechanisms of the central nervous system. More than 50 years ago, the parvicellular neurosecretion, as a concept has been introduced on the basis of studies by what the secretory activity of arcuate neurons into the pituitary portal vessels had been clearly demonstrated. The nucleus consists of a variety of peptidergic and dopaminergic neurons. The vast majority of these neurons have been coded to express more than one neuropeptides and/or neurotransmitters. Up to date, 11 neuropeptides have been demonstrated in the nucleua that may act, depending of their target sites as neurohormones, neuromodulators or neurotransmitters.

Neurons in the arcuate nucleus receive neuronal and humoral inputs. The neuronal signals can be classified as intranuclear (internal organization of cells for common response to proper stimuli), hypothalamic (mainly from the paraventricular, periventricular and ventromedial nuclei, and from cells in the dorsolateral hypothalamic area) and extrahypothalamic inputs (from the viscerosensory nucleus of the solitary tract and brainstem biogenic amine cell groups). Significant afferent signals arise through the blood circulation, especially through the subependymal plexus of the median eminence which branches terminate in the medial part of the arcuate nucleus. This part of the nucleus (especially the arcuate nucleus/median eminence angle) serves as an "open gate" for humoral signals and certain blood-born substances since this part of the nucleus lacks of blood-brain barrier. Furthermore, the penetration of intraventricularly injected neurotropic virus into the medial portion of the nucleus, as well as the presence of supraependymal nerve terminals in this area all indicate that the "gate" is open for proper inputs arising through the cerebrospinal fluid.

The arcuate neurons have a wide spectrum of efferent targets in the brain, including hypothalamic (paraventricular, periventricular, dorsolateral hypothalamic neurons), brainstem and spinal autonomic cell groups. The known functional role of arcuate neurons includes neurosecretory and dopamine controls of certain neuroendocrine activity, like the control of the expression and release of prolactin, gonadotropins and growth hormone in the pituitary gland. Arcuate neurons are sensitive to various stressors. As a response to acute stress, *c-fos* expression can be demonstrated in the arcuate nucleus within minutes after stimuli. The central role of the arcuate nucleus in the regulation of food intake and the energy homeostasis of the body are demonstrated and discussed in detail. Feeding-related peripheral hormones, like insulin, leptin and ghrelin pass the "arcuate gate" and act on neuropeptide Y (NPY)-, agouti-related peptide (AgRP)-, pro-opiomelanocortin (POMC)- and CART-related peptides-expressing neurons. In addition, signals from the upper gastro-intestinal tract may also reach arcuate neurons *via* vagus - nucleus of the solitary tract – ascending pathways to the hypothalamus. The arcuate neurons transfer the food intake-related signals to the efferent loop of the feeding regulatory neuronal circuit (paraventricular and dorsolateral anorexigenic and orexigenic neurons, respectively). In the arcuate nucleus, the alternating inhibitory interactions of NPY/AgRP *versus* POMC/CART neurons serve as a very sensitive and specific balance in feeding.

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