

Small, specific subpopulations of hypothalamic neurons play a major role in regulating the thyroid system

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Regulation of thyroid hormone (TH) levels is a complex multilevel phenomenon. The paraventricular nucleus (PVN) of the hypothalamus

(the region of the brain that controls the involuntary nervous system) has been identified as a direct regulator of thyrotropin (a hormone secreted by the pituitary gland that regulates the production of thyroid hormones). The PVN is a key regulator of TH levels, integrating multiple signaling systems.

Now for the first time, researchers from Boston University Chobanian & Avedisian School of Medicine, have shown that in addition to being critical for regulating thyroid hormone levels, thyrotropin-releasing hormone (TRH) [neurons](#) play a major role in the response to fasting and weight loss.

To test this function, the researchers used a chemogenetic approach (engineering of protein receptors to respond to previously unrecognized small molecules) to either stimulate or inhibit specific neuronal populations. They injected an [experimental model](#) with an adeno-associated virus (AAV) coding for a mutant receptor activated exclusively by an exogenous compound into specific areas of the brain.

By associating this procedure with genetically modified [experimental models](#), the researchers were able to control the activity of TRH neurons in the paraventricular nucleus of the hypothalamus and of agouti-related protein/neuropeptide Y (AgRP/NPY) neurons of the arcuate nucleus of the hypothalamus.

"It allowed us to show that TRH neuron suppression and AgRP/NPY neuron activation play a major role in the organism's response to negative [energy balance](#), such as fasting," explained corresponding author Anthony Hollenberg, MD, the John Wade Professor of Medicine and chair at the School.

According to the researchers, by controlling the activity of these neurons they were able to change the entire endocrine system related to the

thyroid. "Probing deeper into these findings will lead to new knowledge with potential application to metabolic and thyroid-related diseases, such as obesity and central hypothyroidism," adds Hollenberg, who also is physician-in-chief at Boston Medical Center.

These findings appear online in the journal *Thyroid*.

More information: Ricardo H. Costa-e-Sousa et al, Regulation of Thyroid Hormone Levels by Hypothalamic Thyrotropin-Releasing Hormone Neurons, *Thyroid* (2023). [DOI: 10.1089/thy.2023.0173](https://doi.org/10.1089/thy.2023.0173)

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