Researchers catalog dozens of new neuronal subtypes in the hypothalamus

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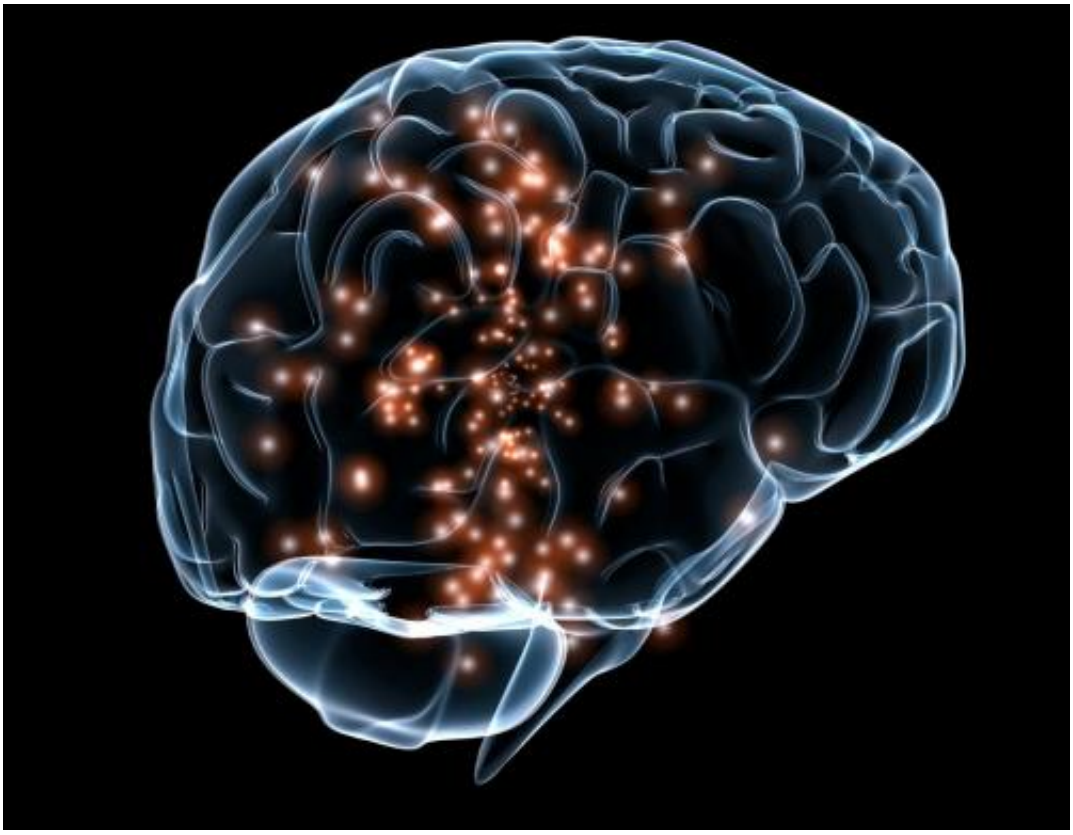

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The human brain is made up of billions of cells. Scientists do not know the identity or exact function of countless thousands of them since comprehensive efforts to catalogue neurons have just recently begun. Studying these many still unidentified cells is an important "hot-spot" in

frontier brain research since it offers the discovery of new cell functions that could play important roles in many diseases. In the Department of Molecular Neurosciences at the Center for Brain Research of the Medical University of Vienna, scientists have now described many previously unknown neurons in the hypothalamus and determined the function of a hitherto uncharted dopamine cell. The study has now been published in the leading journal *Nature Neuroscience*.

An accurate look into the cellular and molecular composition of the brain has recently become possible thanks to a combination of traditional methods, particularly the use of microscopy to determine cellular structure, and "single-cell RNA sequencing". Using the latter method, it is by now possible to extract key molecular information that encodes the identity of each cell – and that means tens of thousands of mRNA molecules per cell.

"The hypothalamus is the area that regulates metabolic processes throughout the body by producing many different hormones. For this reason, it is the region of the brain with the greatest density of structurally and functionally distinct neurons. Considering that as few as 1,000 – 5,000 neurons can control basic hormonal processes such as stress, nutrition and sleep, the discovery of additional neuronal subtypes promises new knowledge to advance our understanding of how fundamental interactions between the brain and the body are triggered and maintained," explains Tibor Harkany, Head of the Department of Molecular Neurosciences within the Center for Brain Research.

The team from MedUni Vienna's Center for Brain Research has distinguished 62 different subtypes of neurons. Thus, it is now possible to investigate their function, including their wiring and modes of communication with other nerve cells locally, as well as in distant regions of the brain. The researchers have already succeeded in identifying the function of a particular subtype of neuron, a dopamine

cell with a unique molecular signature. "We think that the secretion of some hormones (e.g. prolactin) produced in the pituitary gland only occurs when this dopamine cell is inactive. Since its activity changes during the day, it also controls circadian fluctuations in hormone levels," explains Tomas Hökfelt, visiting professor at the Center for Brain Research, who pioneered the anatomical mapping of neuropeptide systems in the hypothalamus. The pituitary gland is a sort of interface, via which the brain regulates processes such as growth, reproduction, sexuality and stress via the release of hormones.

Consequently, it might be possible to exploit these exciting findings to pinpoint drug targets in many of the newly identified neurons in order to intervene in metabolic diseases – for example in obesity, contraception, anorexia, insomnia or even narcolepsy. This line of research expects to predominantly influence metabolic processes through pharmacological modulation of hypothalamic neurons. "These findings could therefore help us to devise new ways of combating many of the most common and devastating diseases in our modern society. Our results encourage us to think that new treatment options might exist, and could target hitherto unknown hormones or receptor systems," explains Roman Romanov, lead author and brain researcher at Medical University of Vienna.

"If we continue to catalogue not only neurons but also other cell types in the brain then we will gain comprehensive insights in how complex functions arise," says Tibor Harkany. "Then it might be possible to precisely explain connections, relationships and interactions between neurons and even predict how, where and when certain neurons act together, even across distant areas of the brain, to orchestrate fundamental outputs throughout life."

More information: Molecular interrogation of hypothalamic organization reveals distinct dopamine neuronal subtypes, *Nature Neuroscience*, nature.com/articles/doi:10.1038/nn.4462

Provided by Medical University of Vienna