Unique design of the neural microcircuit in the ventromedial hypothalamus revealed in mouse model

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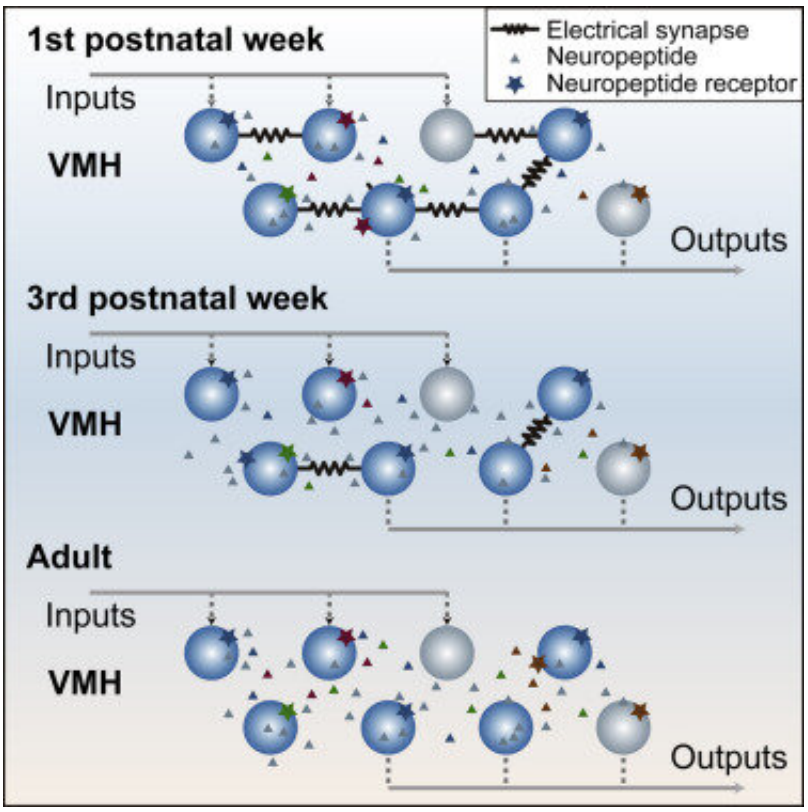

Graphical abstract. Credit: *Current Biology* (2022). DOI: 10.1016/j.cub.2022.05.029

A joint research team led by Dr. Xu Huatai from the Center for Excellence in Brain Science and Intelligence Technology, Chinese

Academy of Sciences, has demonstrated the unique design of the neural microcircuit in the ventromedial hypothalamus (VMH).

Using a mouse model, the researchers applied combinatory approaches to reveal a distinct developmental transition for the neural microcircuit in the VMH. They discovered that the early developmental stage features dense electrical coupling. In contrast, the adult VMH is characterized by sparse chemical synapses as well as prominent neuropeptide transmission. The absence of chemical synapses was further observed in many other hypothalamic nuclei. These findings provide a solid microcircuit basis for a better understanding of hypothalamic functions.

The study was published in *Current Biology* on June 2.

The hypothalamus is a multinucleated structure and internuclear connections have been extensively investigated. However, the innermost hypothalamic nuclei microcircuits have been less examined.

To fill this gap, the researchers made quadruple whole-cell patch-clamp recordings using hypothalamic slices. They first found a high frequency of electrical coupling between neurons during the early development of the VMH, which decreased gradually afterward. The researchers concluded that the electrical synapses were mediated by connexin 36 (Cx36) since conditional knockout of Cx36 in the VMH significantly reduced electrical coupling.

It had been previously discovered that in the neocortex, electrical synapses were the blueprint for chemical synapses. However, from early development to adulthood, chemical synapses were seldom detected by paired recordings in the VMH, indicating sparse intrinsic synaptic connectivity in the adult VMH. Similarly, in other hypothalamic areas, paired recordings only detected a few electrical synapses but no chemical synapses. These observations reveal sparse chemical

connectivity as a generalized feature of the hypothalamic microcircuit.

Paired recordings efficiently detect synaptic connections within a limited range (