An estrogen-responsive module in the ventromedial hypothalamus selectively drives sex-specific activity in females.

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Public Summary:
Estrogen-receptor alpha (ERalpha) neurons in the ventrolateral region of the ventromedial hypothalamus (VMHVL) control an array of sex-specific responses to maximize reproductive success. In females, these VMHVL neurons are believed to coordinate metabolism and reproduction. However, it remains unknown whether specific neuronal populations control distinct components of this physiological repertoire. Here, we identify a subset of ERalpha VMHVL neurons that promotes hormone-dependent female locomotion. Activating Nkx2-1-expressing VMHVL neurons via pharmacogenetics elicits a female-specific burst of spontaneous movement, which requires ERalpha and Tac1 signaling. Disrupting the development of Nkx2-1(+) VMHVL neurons results in female-specific obesity, inactivity, and loss of VMHVL neurons coexpressing ERalpha and Tac1. Unexpectedly, two responses controlled by ERalpha(+) neurons, fertility and brown adipose tissue thermogenesis, are unaffected. We conclude that a dedicated subset of VMHVL neurons marked by ERalpha, NKX2-1, and Tac1 regulates estrogen-dependent fluctuations in physical activity and constitutes one of several neuroendocrine modules that drive sex-specific responses.

Scientific Abstract:
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