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Transcriptomic study reveals changes in gene expressions in the lateral hypothalamic area in socially isolated mice: relevance to drug addiction

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Social isolation (SI) has profound effects on physiological functions and behaviors in animals. As a stressor, SI promotes the development and relapse of drug addiction in humans and animal models. It has been proposed that brain circuitry regulating social homeostasis has a central role in mediating effects of SI on animals. The lateral hypothalamus (LH) is a classic brain center regulating homeostatic processes in animals. We hypothesize that the LH serves as a regulator of social homeostasis and that SI would alter animal behaviors controlled by the LH. To address this question, we examined changes in gene expressions in the LH in mice under acute SI in this study. Group housed male mice (3-4 months old) were randomly divided into two groups: control and SI (mice were separated and singly housed for 24 hours). Brain tissue from the LH area was collected; total RNA was extracted and transcriptomic analysis was performed. Our preliminary results indicated that 895 genes were significantly ($P<0.05$, t test) up-regulated (fold change >1.2) with 402 genes down-regulated (fold change < -1.2) in mice under acute SI. Specifically, up-regulated genes included those encoding proteins responsible for neurotransmitter/modulator receptors, neuropeptides and neuropeptide receptors relevant to drug addiction, such as Hcrt, Trh, Trhr, Crhr1, Th, OPRK1, OPRM1. Synaptic potentiation in glutamatergic synapses on Hcrt cells was also identified. In summary, our results suggest that drug addiction relevant molecular pathways were activated by SI in the LH area, underlying SI-induced drug abuse and relapse in animals and humans.