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Neuronal ATG1 coordinates autophagy induction with physiological adaptations against impaired brain metabolism

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Abstract

In the mammalian brain, hypothalamus integrates metabolic and endocrine signals to evoke physiological responses to food deprivation. This is achieved via regulation of the mTORC1 nutrient sensing pathway. Nevertheless, the relative mechanism is still obscure. Here, we used *Drosophila* and zebrafish to show that, upon nutrients deprivation, mTORC1 inhibition acutely perturbs serotonergic neurotransmission via activation of the protein ATG1. Neuronal ATG1 alters intracellular localization of serotonin transporter, which increases extracellular serotonin and stimulates postsynaptic receptor 5HTR7. These brain alterations enhance food-searching behavior, impede peptidergic secretion, extend longevity and induce systemic catabolism throughout the body, via inhibition of the insulin signaling. Our findings highlight a novel mechanism that orchestrates coordinated physiological responses against reduced brain metabolism and assists survival under conditions of food shortage.