

Regulation of systemic energy homeostasis by serotonin

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Whole body energy balance is achieved through the coordinated regulation of energy intake and energy expenditure in various tissues including liver, muscle and adipose tissues. Although central 5-HT functions as an anorexigenic neurotransmitter in the brain, recent studies suggest the new functions of peripheral serotonin in energy homeostasis ranging from the endocrine regulation by gut-derived serotonin to the autocrine/paracrine regulation by adipocyte-derived serotonin. Pharmacological inhibition of 5-HT synthesis leads to inhibition of lipogenesis in epididymal white adipose tissue (WAT), induction of browning in inguinal WAT and activation of adaptive thermogenesis in brown adipose tissue (BAT). Fat specific *Tph1* knock-out (*Tph1* FKO) mice exhibit similar phenotypes as mice with pharmacological inhibition of 5-HT synthesis, suggesting the localized effects of 5-HT in adipose tissues. In addition, *Htr3a* KO mice exhibit increased energy expenditure in BAT and *Htr2a* KO mice exhibit the decreased lipid accumulation in WAT. These data suggest the clinical significance of the peripheral serotonergic system as a new therapeutic target for anti-obesity treatment.