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.