

## Serotonin and obesity

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The purpose of feeding is to restore the caloric homeostasis within the body (the balance between energy supply and energy expenditure). This process controlled by many central and peripheral physiological mechanisms within the human body.<sup>[1]</sup>

The central mechanisms which control food intake involve many CNS regions and including different neurotransmitters and neuropeptides. Of these neurotransmitters, is serotonin (5-hydroxytryptamine).<sup>[2]</sup>

The mechanism, through which, serotonin control food intake is not fully understood. However, there is evidence suggests that serotonin enhance melanocortin 4 receptors (MC4) which is involved in food intake control in the hypothalamus.<sup>[3]</sup>

The relationship between serotonin and feeding, dated back to the 1970s, were scientists found that there is inverse relationship between serotonin level and food intake.<sup>[2,3]</sup> From that time, many anti-obesity drugs were developed that modulate serotonin level, but regrettably most of them withdrawn because of their serious adverse effects like fenfluramine and lastly sibutramine.<sup>[4]</sup>

Researchers nowadays convinced that the adverse effects of these drugs are due to non-selective action on serotonin receptors.<sup>[5]</sup> There are three serotonin receptors implicated in the control of food intake and body weight control includes 5-HT<sub>1B</sub>, 5-HT<sub>2C</sub>, 5-HT<sub>6</sub>.<sup>[6]</sup> Other receptors which are responsible for the harmful effects include 5-HT<sub>1A</sub>, 5-HT<sub>2A</sub>, 5-HT<sub>2B</sub> receptors.<sup>[7]</sup>

Lorcaserin is a highly selective 5-HT<sub>2C</sub> receptor agonist that holds promise in the treatment of obesity. However because of its marginal effects (benefit to risk ratio) and issues regarding carcinogenicity in animals, Lorcaserin may be not the ideal drug for treatment of obesity.<sup>[8]</sup>

5-HT<sub>6</sub> receptors distributed predominately in the CNS, these receptors has the ability to modulate dopaminergic and cholinergic transmission, authors believe that these receptors

involved in wide range of activities from cognition to depression to anxiety.<sup>[9]</sup>

Recently, in experimental studies, 5-HT<sub>6</sub> receptor antagonist, found to be highly effective in reducing food intake and body weight, therefore these drugs may bring hope to the development of safe and effective drug in the treatment of obesity.<sup>[3]</sup>

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