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Commentary

Mimecan: A Newly Identified Adipokine and Regulator of Appetite

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Originally adipose tissue was considered a site of energy storage, providing mechanical as well as heat insulation and playing a role in the regulation of thermogenesis. However, since the discovery of Leptin in 1994 adipose tissue is now also recognised as an endocrine organ that produces a multitude of substances referred to as "adipokines". These include adipolin, adiponectin, interleukin-6 (IL-6), leptin, omentin, tumour necrosis factor alpha (TNFα) and visfatin which play important roles in the regulation of food intake and metabolism (Smitka and Maresova, 2015). Adipose tissue is currently considered the largest endocrine organ secreting a multitude of hormones and cytokines known to affect processes both within the peripheral and central nervous system.

With respect to leptin and food regulation the adipose tissue acts as a 'safety valve' controlling the long term regulation of food intake. Leptin is released in proportion to the degree of adiposity and reduces food intake when energy reserves are sufficient. Unfortunately, in chronic high fat diet induced obesity the 'safety valve' malfunctions, with the occurrence of leptin resistance in the hypothalamus exacerbating the problem of obesity (Munzberg et al., 2004). Therefore, as a central target for the treatment of obesity, leptin and leptin analogues have proved disappointing as possible pharmacotherapies. The study by Cao et al. (2015) revealed that mimecan, first identified in the organic matrix of bovine bone, is also expressed in adipose tissue and is a potential target for the treatment of obesity. Cao et al. (2015) described mimecan as a satiety hormone with both intraperitoneal and intracerebroventricular injections suppressing food intake. Information on whether this is due to changes in meal size or meal frequency is unavailable but the cumulative effects of mimecan on food intake appear to be considerable. Cao et al. (2015) demonstrated that the anorexic effects of mimecan are independent from leptin and melanocortin signalling with data showing a reduction in food intake still observed in obese leptin receptor knockout mice (db/db mice) and Agouti mice (A^Y/a mice) respectively. Cao et al. (2015) suggest mimecan-induced anorexia, within the central nervous system, is probably mediated via interleukin 1β (IL-1 β) and IL-6. It is known that IL-6 production occurs selectively in microglia rather than astrocytes and primary hypothalamic neuronal cells and therefore the study by Cao et al. (2015) supports the emerging evidence for microglia mediated anorexic effects (Le Foll et al., 2015). Microglia and astrocytes may prove to be critical in appetite regulation within the central nervous system with the potential to be new novel targets for the treatment of obesity.

There are still many questions to be answered before the importance of mimecan in food intake and appetite regulation can be determined. These include translation of findings in the mouse to the human and establishment of the effectiveness of mimecan on food intake in high fat diet induced obesity. For instance, leptin is effective at reducing food intake in leptin knockout mice (ob/ob mice) (Halaas et al., 1995) and also obese humans with defective leptin production (Paz-Filho et al., 2011). It is only in diet-induced obese conditions that leptin resistance is observed. It is therefore essential to establish the effectiveness of mimecan at reducing food intake in high fat diet induced obese mice. In addition, although the effect of mimecan on food intake is promising there appears to be desensitisation to mimecan over treatment days raising some doubts on the usefulness of mimecan as a pharmacotherapy for obesity.

Cao et al. (2015) reason that, as lower concentrations of mimecan were required to elicit an anorexic effect via intracerebroventricular compared to intraperitoneal injections, mimecan is acting centrally. They discount any possible peripheral effect. It would be useful to know the circulating levels of mimecan after intraperitoneal injections in addition to the clearance rates. It is known that numerous adipokines are expressed in other peripheral regions associated with satiety signalling, such as the gastrointestinal tract. For example, leptin is not only expressed in adipose tissue but also the stomach where it modulates vagal afferent satiety signals (Kentish et al., 2013). Cao et al. (2015) demonstrated that mimecan is expressed in other organs and tissue such as the lungs but did not look at expression in the gastrointestinal tract where the short term regulation of food intake and meal size is initiated. It would be interesting to see if specific regions within the gastrointestinal tract express mimecan.

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In conclusion, mimecan is an adipokine hormone that induces anorexia centrally by increasing IL-1β and IL-6 in the hypothalamus. The role mimecan plays in the regulation of food intake in high fat diet induced obesity and the therapeutic potential of mimecan or analogues of mimecan in the treatment of obesity remains to be determined.

The author declares no conflict of interest.

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