Studying the role of the vagus nerve in dietary obesity development and treatment

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Abstract (600 word limit)

The purpose of this review is to highlight the role of the vagus nerve in obesity and how it can be treated therapeutically with neuromodulation or pharmacology. An important role of the vagus nerve innervating the gut is to control metabolism. A-fibres can be further broken down into four subgroups with slightly different diameters, myelination and conduction velocities. The vagal fibres transmit information bidirectionally between the brain and peripheral organs. This cell is responsible for communicating peripherally with the brain about the amounts and types of nutrients. There are two types of neurochemical phenotypes expressed by vagal afferent neurons depending on nutritional status, regulating whether food intake is inhibited or stimulated. Chronic consumption of calorie-rich diets reduces the sensitivity of vagal afferent neurons to peripheral signals and their constitutive expression of orexigenic receptors and neuropeptides. As a result, vagal afferent signalling is disrupted, resulting in hyperphagia and obesity. As well as neuromodulation of the vagus nerve, obesity can also be treated with it. Vagal nerve stimulation prevents weight gain in response to a high-fat diet, although the mechanisms are unclear. However blunt the tools are available to distinguish afferent and efferent signaling to different organs, it is clear that subdiaphragmatic vagal afferent fibers provide negative feedback to regulate meal size. In the gastrointestinal tract, mechanosensitive vagal afferent terminals suppress meal size in response to distension, and chemosensitive vagal afferent terminals suppress meal size in response to nutrient types and quantities. Vagal nerve stimulation has been proven to promote weight loss in patients with depression or epilepsy in small clinical studies. Significant weight loss results from blocking the vagus nerve through vagal blockade. These techniques have significant limitations. The problem is that these approaches fail to distinguish between efferent and afferent signalling, which may act in opposition to each other, thereby masking a crucial effect of either in energy homeostasis. The VNS has been described as controlling body weight via multiple mechanisms. Some studies reported a significant reduction in food intake, while others detected an increase in energy expenditure. The relative importance of either feeding for body weight after VNS treatment has not yet been tested in pair feeding experiments. None of these approaches targets vagal fibres innervating individual organs selectively, and since multiple organs may send opposing signals, ablating all signals from multiple organs may mask the importance of a specific organ. The reason for the mild to moderate pain with VBLOC was not discussed, but likely stemmed from the onset response, which causes unwanted vagal efferent muscle contractions and nociceptive vagal afferent signalling to the brain. In light of the effects of VNS on pain perception, it has been hypothesized that repeated periods of hypersensitivity to painful stimuli may result from acute stimulation. In view of the growing evidence described above and its location in a peripheral area, the vagus nerve is a promising pharmacological target for treating obesity. The vagal afferent neurons and their terminals, as well as the vagal efferent preganglionic terminals, are situated outside the blood–brain barrier. It is possible to design drugs to target the vagus nerve that are too large to cross the blood-brain barrier without causing unwanted side effects due to off-target interactions at central sites. Additionally, these techniques indiscriminately block anorexigenic and orexigenic signals, which might obscure the importance of one signal over another. As a putative mechanism, vagal blockade inhibits aberrant orexigenic signals arising in obesity, which may explain its weight-loss effects. Future pharmacotherapies targeted at the vagus nerve for the treatment of obesity are discussed in terms of approaches and molecular targets. Finally, the vagus nerve is proving to be an attractive target for the treatment of obesity thanks to strong evidence suggesting it is involved in the development of obesity.

Importance of Research:

There is bidirectional communication between the brain and peripheral organs through the vagus nerve. In the gut, vagal efferents are involved in digestion and absorption, while vagal afferents provide negative feedback to the brain about the volume and type of nutrients to inhibit food intake. It is not simply that vagal afferent neurons relay signals to the brain, but they also integrate these peripheral signals in order to inform decisions about previous meals. A disruption of vagal afferent neurons in obesity and the positive effects of neuromodulation on obesity raise the possibility that pharmacological agents that selectively target the abdominal vagus nerve could be effective in treating obesity. Further studies of the vagus nerve in obesity are warranted based on our current understanding. Future work should focus on developing better tools to study afferent and efferent neuron subpopulations, as well as more detailed investigations to determine the extent to which these subpopulations contribute to obesity and how to restore normal electrophysiological and neurochemical function in obesity. The vagus nerve alone may not be sufficient to reverse obesity, but due to the low level of side effects associated with selective vagal therapies like neuromodulation, as well as their theoretical pharmacology, these therapies could be used in conjunction with other treatments.

Information of Institute:

In Edmonton, Alberta, Canada, the University of Alberta, also known as U of A or UAlberta, is a public research university. Henry Marshall Tory, the university's first president, and Alexander Cameron Rutherford, the first premier of Alberta, founded it in 1908. This was made possible by the Post-secondary Learning Act. The university is considered a "comprehensive academic and research university" (CARU), which means that it offers a range of academic and professional programs leading to undergraduate and graduate degrees. Edmonton has four campuses, Camrose has an Augustana campus, and downtown Calgary has a staff centre. Originally, the north campus consisted of 150 buildings covering 50 city blocks across the North Saskatchewan River valley from downtown Edmonton. Over 39,000 students from Canada and 150 other countries participate in 400 programs across 18 faculties. The University of Alberta drives the economy in Alberta. According to estimates, it affects Alberta's economy by $12.3 billion annually, or five percent of the province's GDP. Through the University Act, passed during the first session of the then-new Legislative Assembly with Premier Alexander C. Rutherford as its sponsor, the university was chartered in 1906 as a single, public, provincial university.

Recent Publications (minimum 15)

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Biography (200 word limit)

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William Johnson with a PhD in Molecular Biology. My experience includes managing projects, conducting research, and teaching. Molecular genetics has been a focus of my expertise. In addition, I have contributed to the development of biotechnology programs in both public and private companies. Currently, I am working at the University of Alberta, Canada. I am studying the role of the vagus nerve in the development and treatment of dietary obesity.

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