

Research report

Vagus nerve stimulation acutely alters food craving in adults with depression

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Received 21 June 2006; received in revised form 17 July 2006; accepted 19 July 2006

Abstract

Vagus nerve stimulation (VNS) is now available as a treatment for epilepsy and treatment-resistant depression. The vagus nerve plays a central role in satiety and short-term regulation of food intake and research suggests a relationship between VNS and weight loss. The underlying mechanisms of this relationship are unknown. The purpose of the current study was to determine whether acute cervical VNS might temporarily alter food cravings. Thirty-three participants were recruited for three groups; depression VNS, depression non-VNS, and healthy controls. Participants viewed 22 computerized images of foods twice in one session and completed ratings for food cravings after each image. The VNS participants' devices were turned on for one viewing of an image and off for the other (randomized order). Participants were blind to VNS condition (on versus off). Acute VNS device activation was associated with a significant change in cravings-ratings for sweet foods. A significant proportion of variability in VNS-related changes in cravings was accounted for by patients' clinical VNS device settings, acute level of depression, and body mass. Further studies are warranted addressing how acute or chronic VNS might modify eating behavior and weight.

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Keywords: Vagus nerve stimulation; VNS; Obesity; Food cravings; Brain stimulation; Depression

Introduction

Vagus nerve stimulation

Clinicians are investigating several new brain stimulation techniques, such as vagus nerve stimulation (VNS), to treat psychiatric disorders including depression, anxiety, and bipolar disorder (Marangell et al., 2002; Mu et al., 2004; Nadkarni, LaJoie, & Devinsky, 2005; Rush et al., 2000; Sackeim et al., 2001). The vagus nerve, one of 12 cranial

nerves, carries information to and from the brain to major organs including the heart, stomach, lungs and esophagus. Electrical stimulation of the vagus afferents (information traveling to the brain from the body) results in activation and/or inhibition of brain stem structures such as the medulla and the nucleus of the tractus solitarius (NTS) (George et al., 2000). These inputs are then conveyed to widespread bilateral areas of the cerebral cortex, diencephalon and limbic lobe (Bohning et al., 2001; Chae et al., 2003; Henry, 2002; Lomarev et al., 2002; Mu et al., 2004).

VNS involves implantation of a small generator under the skin overlying a patient's chest. An electrode is threaded from the generator subcutaneously and attached to the left-cervical vagus nerve. By placing a computer-controlled magnetic wand over the chest of a patient with a VNS implant, a clinician can adjust various parameters of

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the stimulation including the output current intensity (mA), the frequency (Hz), the pulse-width (μ s), stimulus on-time (seconds) and stimulus off-time (minutes). Various VNS stimulation parameters have been associated with activation of different brain areas (Lomarev et al., 2002; Mu et al., 2004).

VNS was initially approved by the Federal Drug Administration (FDA) as a treatment for intractable epilepsy (Tecoma & Iragui, 2006; Uthman, 2000). Since its approval, VNS has been investigated for several other clinical applications including depression (Marangell et al., 2002; Mu et al., 2004; Rush et al., 2000; Sackeim et al., 2001), and chronic pain (Borckardt, Kozel, Anderson, Walker, & George, 2005). VNS has recently received FDA approval as a treatment for treatment-resistant depression (George et al., 2000; Rush et al., 2000, 2003; Sackeim et al., 2001).

Vagus nerve stimulation and weight change

There has been a growing interest in the use of VNS to study and treat obesity (Roslin & Kurian, 2001; Sobocki et al., 2001). This is an especially important area of research given that 65% of Americans are overweight or obese (Hedley et al., 2004). VNS is a logical choice for study because the vagus nerve has long been linked to neurological systems associated with hunger and satiety and it plays a central role in the short-term regulation of food intake (Havel, 2001). There is evidence, in animals and humans, that neurostimulation interventions (like VNS) can be used to impact eating behavior and weight loss (Burneo, Faught, Knowlton, Morawetz, & Kuzniecky, 2002; Cigaina, 2002; Roslin & Kurian, 2001; Sobocki, Krolczyk, Herman, Matyja, & Thor, 2005).

Experimental research with animals has found that stimulation of the vagus nerve, both through thoracotomy and laparotomy access, has an influence on food intake and body weight (Sobocki et al., 2005). In a study with normal weight mongrel dogs, chronic intermittent high-dose VNS within the thorax resulted in substantial weight loss. The dogs took longer to consume their food and failed to finish the food on their plate, an unusual phenomenon for this type of dog (Roslin & Kurian, 2001). In another study with animals, Sobocki and colleagues found VNS (stimulation of the abdominal part of the vagus nerve) was associated with a significant difference in body mass in a sample of non-obese pigs. There was a significantly different change in the ratio of fat for the pigs that received VNS versus the pigs that did not, but no effect on metabolism was found. Results of this study suggest that VNS reduces body mass in animals specifically through its influence on decreasing fat stores (Sobocki, Fourtanier, Estany, & Otal, 2006). Overall, the past research examining VNS in animals demonstrates that VNS affects eating behaviors, weight, and body composition, although the majority of these studies stimulated the vagus closer to the stomach than is done with cervical VNS used in humans.

Few studies examining cervical VNS and weight have been conducted in humans. In patients who received cervical VNS for the treatment of epilepsy, 62% experienced significant weight loss. In this sample ($N = 27$), the patients with higher output settings for the VNS device were more likely to lose weight (Burneo et al., 2002). It is not known whether this VNS-related weight-loss was caused by changes in metabolism, decreases in fat stores, changes in hunger and/or satiety signaling in the brain, changes in food cravings, or by some other mechanism. In the pivotal study of VNS in treatment-resistant depression, there was no effect on weight (Rush, Marangell et al., 2005; Rush, Sackeim et al., 2005). More research is needed to understand the relationship between VNS and weight change in humans.

Mood and eating behaviors

The relationship between mood and eating behaviors has long been of interest to researchers (Canetti, Bachar, & Berry, 2002). Studies have sought to examine how mood affects not only the amount of food consumed but also the types of foods eaten. Lyman (1982) found that individuals were more likely to consume healthy foods during positive emotions and more likely to consume unhealthy foods when experiencing negative emotions. Other research suggests that the meals eaten when experiencing positive or negative moods are larger in portion than those eaten during a neutral mood (Patel & Schlundt, 2001). More recent research has focused on understanding the role of specific mood states in eating and food cravings. Certain moods, such as anger or joy, have been found to have a greater influence on eating than sadness or fear (Macht, 1999). Depressive symptoms in individuals are associated with higher BMIs, more eating concerns, and lower self-esteem (Werrij, Mulkens, Hospers, & Jansen, 2006). Recently, Killgore & Yurgelun-Todd (2006) found that affect differentially predicted regional cerebral responses to high versus low calorie foods. Their research suggests that there may be a neurobiologic substrate underlying the tendency for increased food cravings found for high-calorie foods during heightened negative emotions. In summary, this research demonstrates that mood affects food cravings and the amount and types of food consumed.

Purpose and aims of the current study

The current project sought to investigate whether acute left cervical VNS might temporarily affect food cravings in patients with chronic, treatment-resistant depression. As past research with animals and humans demonstrates, VNS is associated with changes in eating behaviors and weight (Burneo et al., 2002; Sobocki et al., 2005). However, does left cervical VNS alter metabolism or decrease food cravings? Currently, there are no published studies that have systematically investigated the effects of left cervical VNS on food cravings in humans. Examining the acute

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