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How eating affects mood

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ABSTRACT

IOAKIMIDIS I, M. ZANDIAN, F. ULBL, C. BERGH, M LEON, AND P. SÖDERSTEN. How eating affects mood. PHYSIOL BEHAV 2011 (000) 000–000. We hypothesize that the changes in mood that are associated with eating disorders are caused by a change in eating behavior. When food is in short supply, the rhythm of the neural network for eating, including orbitofrontal cortex and brainstem, slows down and we suggest that this type of neural activity activates a partially overlapping neural network for mood, including dorsal raphe serotonin projections to the orbitofrontal and prefrontal cortex. As a consequence, people who restrict the amount of food that they consume, either by choice or by their limited access to food, become preoccupied with food and food-related behavior. Most eating disorders emerge from a history of dietary restriction and we suggest that disordered eating consequent upon food restriction produces the altered mental state of patients with eating disorders. Based on the present hypothesis, eating disorders are not the result of a primary mental disorder. Rather, this notion suggests that the patients should be treated by learning to eat an appropriate amount of food at an appropriate rate.

1. Introduction

Improving outcome in anorexia and bulimia nervosa and other eating disorders is desirable as many interventions have suboptimal effects [1,2]. A possible reason for the limited success is because the symptoms which are targeted may not be causally related to eating disorders. For example, therapies that alleviate anxiety or depression in patients without eating disorders are not effective in patients with eating disorders [3]. We offer an alternative hypothesis according to which disordered eating *causes* changes in mood by activating the 5-hydroxytryptamine (5-HT, serotonin) projections from the dorsal raphe nucleus to the orbitofrontal and prefrontal cortex, suggesting an alternative way to treat these patients.

In this review, we will first describe our perspective on the etiology and treatment of eating disorders. We then discuss the effects of dietary restriction on mood and eating behavior, followed by a discussion of the neurobiology of eating that will describe the overlap of that system with the neural system that is engaged in mood. A discussion of how eating and mood are causally related will follow, along with a suggestion of how such a relationship may be disrupted by pharmacological treatment. We then suggest how the hypothesis can be tested and put into clinical use. Finally, we mention some limitations of the hypothesis.

2. A framework for understanding eating disorders

> "A framework is not a detailed hypothesis or set of hypotheses; rather, it is a suggested point of view for an attack on a scientific problem, often suggesting testable hypotheses … A good framework is one that sounds reasonably plausible relative to available scientific data and that turns out to be largely correct." [4]

We have previously described a framework for the development and maintenance of anorexia nervosa [5]. Briefly, there are two known risk factors for anorexia nervosa, dieting and enhanced physical activity. Experiments on animals had demonstrated that both of these risk factors activate mesolimbic dopamine neurons and locus coeruleus noradrenaline neurons that are thought to play a role in reward and selective attention, respectively [5]. Hence, we suggested that anorexia develops because it is initially rewarding to eat less food and be physically active when the dopamine reward system is engaged and that anorexic behavior is subsequently maintained by conditioning to the situations that provided the reward when the noradrenaline attention system is activated [5]. In an update of this hypothesis, we provided information on how dietary restriction influences both behavior and neuroendocrine function, we described the brain mechanisms of reward and attention in further detail, and presented an experimental analysis of how hormones and behaviors are interrelated in anorexia nervosa [6,7]. A new study has confirmed our prediction that the dopamine innervations of the forebrain are engaged in anorexia nervosa [8]. Another study confirmed that the

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locus coeruleus noradrenaline neurons are activated when contextual cues induce a conditioned response [9] and yet another new study pointed out that such cues refer to the environment in which the learning event takes place [10]. Contextual cues play a significant role in both eating behavior [11,12] and eating disorders [13].

Although these studies have added plausibility to the framework that we have used to understand the onset and maintenance of anorexia, we have been reluctant to speculate on the means by which the brain produces the emotional problems associated with anorexia. Our aim is to fill this gap by explaining how eating behavior influences mood by connecting the brain and the mind, thus adding an essential part to the framework.

3. Restricted food intake and emotional responses

> "What I was not expecting was the effect it would have on the mind, the total feeling of depression and the total occupation with the idea of food…" A participant in a starvation experiment [14].

The effects of voluntary or enforced food restriction on mood and behavior were documented long ago [14,15]. Thus, if the availability of food is reduced, people start thinking only about food, they will become entirely concerned with finding food and eventually they will experience depression, anxiety among other emotional symptoms [15]. Also, they eat slowly; "Toward the end of starvation some of the men would dawdle for almost two hours over a meal which previously they would have consumed in a matter of minutes." [14]. These emotional and behavioral effects of voluntary or involuntary food restriction have been described in hundreds of thousands of people and the similarities with anorexia are compelling [6,14,15].

How does the brain turn food restriction into serious mood and behavioral states? The role of the brain in the functional changes that occur when someone is deprived of food should be characterized as permissive, rather than controlling. This distinction is important, as we have found that while the hypothalamic messenger neuropeptide Y increases food intake if infused into the brain of rats when food is easily available, it has the opposite effect when the availability of food is restricted [6]. The physiological ambiguity of neuropeptide Y suggests that the brain has a subtle role in the sequence of events that evolve when the supply of food is reduced.

4. The neural engagement in eating and mood

A pattern generator for chewing and swallowing is located between the caudal facial nucleus and the trigeminal motor nucleus in the brainstem [16,17]. If experimentally isolated from input, its inherent rhythm is expressed in the presence of excitatory amino acids [16], but the rhythm is normally modulated by sensory input which can be communicated via adjacent brain regions such as the serotonin cells of the raphe nuclei [16,18,19]. Thus, while serotonin neurons in the dorsal raphe are activated during chewing and licking [20], serotonin neurons in the caudal raphe are activated during swallowing [21]. These brainstem areas, and additional hypothalamic areas, along with the orbitofrontal and prefrontal cortex, make up a neural network with bidirectional connections that are engaged during eating [shown by the blue lines in Fig. 1].

Eating behavior emerges in rhythmic bursts when neonates are suckling, and this behavior is transformed into the rhythmic muscular activities of chewing and swallowing [22]. Normal eating behavior in adults is characterized by an initial rapid rate of eating, eventually followed by a decelerated rate of eating over the course of a meal as the individual approaches satiety [23].

The neural pattern generator for chewing and swallowing and the neighboring serotonin neurons innervate the orbitofrontal and prefrontal cortex and other limbic forebrain areas [18,24,25]. Cortical activity during chewing activates the ascending serotonin neurons in the dorsal raphe nucleus [26,27] that project to the orbitofrontal and prefrontal cortex and thereby *causes* mood changes [27–29; shown by the red arrows in Fig. 1]. These may include mood and hedonic changes associated with vomiting [30,31], importantly involved in eating disorders. Food is a major entrainer of circadian rhythms [32], food restriction is a potent arousing stimulus, which may phase shift circadian rhythms via the same dorsal raphe serotonin projections [33]. Interestingly, the availability of food during the course of a day can change the temporal expression of eating [34,35], producing mood changes [36,37]. Equally interesting, many of the endocrine and metabolic derangements in an experimental model of this situation are reversed by re-entrainment of the rhythm by food [38].

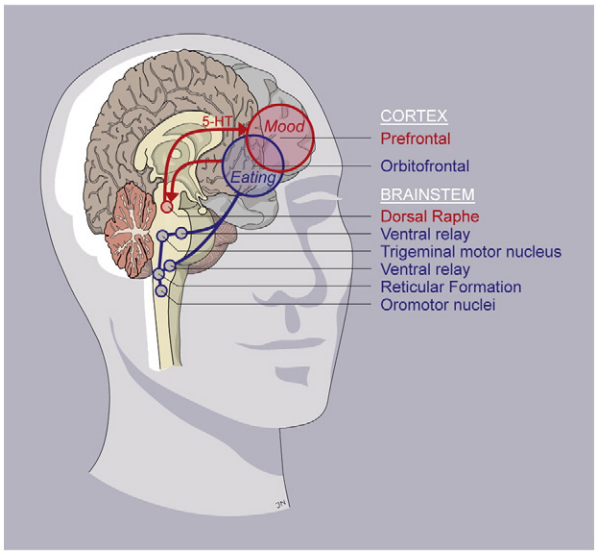

Fig. 1. The neural engagement in eating including orbitofrontal and prefrontal cortex and brainstem areas, shown in blue, which are hypothesized to mediate changes in mood via the serotonin (5-HT) projections of the dorsal raphe to the prefrontal cortex, shown in red. Lines without arrows indicate bidirectional connections.

Normal activation of this neural network is associated with positive emotions. For example, breastfeeding has a calming effect on both the mother and her baby; by sucking on the nipple, the newborn rat activates the neural network of emotion in the mother and, very likely, also in itself; thereby promoting a strong emotional bond between the two [39]. In the adult, chewing activates parts of the same brain network [25,26] and has a relaxing effect [40]. However, experimental damage of this network can cause both chewing disorders and anxiety [18]; mood disorders are common among patients with bruxism and other disturbances of the muscles used for chewing [41] and patients with eating disorders can suffer from bruxism [42]. Indeed, disruption of normal mastication was recently suggested to account for cognitive decline in aging and dementia [43,44]. Thus, when chewing goes wrong, mood and cognitive disorders seem to emerge. Conversely, food-restricted volunteers often used large amounts of chewing gum, possibly to alleviate the depression and anxiety they experienced in the food deprived condition by restoring normal levels of mastication [14]. A recent study supports this possibility by showing that chewing gum reduced anxiety in response to an external stressor [45].

The proposed eating network and the mood network share areas of the brain that support a variety of functions, such as the cortical masticatory areas [46,47], the brainstem pattern generator for eating [17,48–50], the motoneurons related to eating [51], the orbitofrontal cortex [52], and the serotonin neurons that are involved with cognition,