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. PHYSIOLO 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.

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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. 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.

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 coerulescent 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
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,
emotion and aggression [28,29,53–55]. Given the shared neuroanatomy, we hypothesize that both positive and negative emotions can be caused by changes in eating behavior.

5. Mastication and the mind

We make up our mind before we do something; thought precedes action. The cause of eating disorders is often analyzed in a similar way; altered states of mind, such as anxiety and mood disorders are thought to predate and therefore cause eating disorders [3]. However, both events may have a common cause, and although mental states often correlate with behavior, the correlation is not necessarily causal. While research has suggested that state of mind and action can be dissociated experimentally [56], an individual is often convinced that a change of mind caused the change in behavior. The intention to act is taken for granted also when the behavior of others is considered; a mental cause is offered as an explanation even after the action has occurred [56,57]. The argument of mental causation is compelling, but on occasion the mind draws conclusions about cause-effect relationships that do not exist [56,57].

We suggest that mood changes in eating disorders are effects of disordered eating and the associated mental changes are state-dependent emergent properties. In fact, the evidence for the hypothesis that eating disorders are caused by pre-existing mental disorders [3] has been questioned in two comprehensive reviews [58,59]. We also suggest that the cognitive changes in eating disorders and during shortage of food are realistic; one should be concerned if little food is available and more concerned, perhaps even “obsessed” with food as the shortage persists. Mind and action need to be coupled; there are many clinical examples that patients feel out of control if they are not [56].

6. Why pharmacological treatment fails

The cell bodies of the serotonin neurons in the brainstem, which are part of the neural network for eating and emotion, express 5-HT1A receptors [24], which mediate many of the effects of serotonin on emotion and cognition [24,29]. These receptors are the target of selective serotonin reuptake inhibitors (SSRIs), which are successfully used to treat depression and anxiety [24,29]. However, SSRIs are ineffective in treating either the disordered eating behavior, the depression, or the obsessive behavior typically associated with eating disorders [3]. SSRIs can unfortunately cause chewing disorders [60] probably by affecting the serotonin-innervations of the brainstem cholinergic motoneurons involved in chewing [51,61,62], perhaps further exacerbating the difficulties that anorexics have while eating and these drugs may therefore enhance, rather than alleviate anxiety and mood disorders in those patients.

Interestingly, the 5-HT1A receptor has a role in the ontogeny of neural networks that support behavioral rhythms; stimulation of the receptor by SSRIs can disrupt normal development, thereby causing both rhythm disorders [63] and emotional disorders [64] in adulthood. These disorders are characterized by a slowing of the behavioral rhythm [63,64], exactly what is seen with the slowing of the eating rhythm in long term food restriction [14].

7. Testing the hypothesis

Because eating behavior has a proposed causal role in producing anxiety and mood disorders, varying the speed of eating and examining both dorsal raphe serotonin neuron activity and anxiety in experimental animals would test the hypothesis. Conversely, the hypothesis predicts that activity in the brainstem-to-cortex serotonin projections should have a minor effect or no effect on eating behavior. It is noteworthy, that the dorsal raphe serotonin pathways to the cortex, which have a central role in the present hypothesis, are sexually dimorphic [65]. Whether this sex difference is related to the marked sex difference in anorexia remains to be determined. Further testing of the hypothesis should involve studies on the interconnections among the raphe serotonin neurons in the brainstem and their projections to other brain areas engaged in eating, as well as the interrelation among the cortical areas involved with both mastication and mood.

Thus, the aim of the present hypothesis is to place eating behavior and mood into neurobiological context. Cognitive and emotional models of eating behavior, by contrast, often do not take the brain into consideration [66,67] postulating “cognitive processes” which control how people eat that are independent of physiology [23,68].

“Such models may have little resemblance to the way the brain actually behaves is not seen as a serious criticism. If it describes, in a succinct way, some of the psychological data, what can be wrong with it? Notice, however, that by using such arguments, one could easily make a good case for alchemy or for the existence of phlogiston.” [69]

The quote above [69] reminds us that models of behavior emancipated from neurobiology are at risk of creating both a dualistic problem and a validity problem. Cognitive explanations of eating disorders have not been fruitful and may continue unrewarded unless they relate realistically to the normal functions of the brain.

8. Implementing the hypothesis clinically

In line with the present point of view, re-learning how to eat normally is part of our treatment for eating disorders [70]. We have reported that practising eating at the default decelerated rate normalizes cognitive function [68] and validated our method clinically [71]. Importantly, practising eating at a normal rate is a critical aspect of an effective method for treating anorexics, a method that not only normalizes the disordered eating behavior, but also eliminates the anxiety and depression associated with the disorder [70]. A reduced food intake is a cause not only of anorexia, but also bulimic behavior, because bulimics restrict their food intake until they cannot resist bingeing on available food [72]. Their disorder is similarly effectively treated by normalizing their disordered eating behavior [70]. The treatment has been found to be effective in a randomized controlled trial, bringing 75% of a group of 168 patients into remission in on average 14 months, and preventing relapse within one year in 93% of a group of 83 patients [70]. Regaining the proper pattern of eating appears to be the critical factor in the treatment. A randomized controlled trial comparing the outcome in a group of patients who practice eating at the normal decelerated rate [23] with the outcome in another group of patients who do not practise eating is an important step in translating the present hypothesis into clinical practise.

9. Limitations

This model, of course, does not inform us about the reason why the eating pattern becomes disordered in some individuals and not in others, nor does it explain how eating behavior fails to self-correct when it becomes disordered. Also, it does not account for the marked sex difference in the prevalence of eating disorders. At the same time, however, the model points to the successful intervention that is capable of normalizing both the disordered eating patterns and the disordered emotions that follow food restriction.

The neurobiological support for hypothesis presented here is derived from a mixture of animal and human studies and although the link between the two is not always possible to make, the comparative approach has proven particularly useful in the case of eating and the associated hedonic responses and moods [31]. In addition, there is a considerable amount of direct support from human studies that the serotonin innervation of the prefrontal cortex is involved in mood as outlined in the hypothesis, although activation of this neural substrate...
was achieved in a different manner than chewing in these studies [73]. Obviously, as with any hypothesis, the present hypothesis is in need of testing.

**Conflict of interest statement**

C Bergh and P Södersten each have 28.35% and M Leon has 3% of the stock in Mando Group AB. The Section of Applied Neuroendocrinology, Karolinska Institutet, provides the research basis for the clinical work at Mando Group AB.

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