Progress in Neuro-Psychopharmacology & Biological Psychiatry 80 (2018) 132–142

Contents lists available at ScienceDirect

Progress in Neuro-Psychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp

Neuroendocrinology and brain imaging of reward in eating disorders: A possible key to the treatment of anorexia nervosa and bulimia nervosa

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ARTICLE INFO

Article history:
Received 30 December 2016
Accepted 28 February 2017
Available online 1 March 2017

Keywords:
Anorexia nervosa
Brain imaging
Bulimia nervosa
Eating disorders
Neuroendocrinology
Reward

ABSTRACT

Anorexia nervosa and bulimia nervosa are severe eating disorders whose etiopathogenesis is still unknown. Clinical features suggest that eating disorders may develop as reward-dependent syndromes, since eating less food is perceived as rewarding in anorexia nervosa while consumption of large amounts of food during binge episodes in bulimia nervosa aims at reducing the patient's negative emotional states. Therefore, brain reward mechanisms have been a major focus of research in the attempt to contribute to the comprehension of the pathophysiology of these disorders. Structural brain imaging data provided the evidence that brain reward circuits may be altered in patients with anorexia or bulimia nervosa. Similarly, functional brain imaging studies exploring the activation of brain reward circuits by food stimuli as well as by stimuli recognized to be potentially rewarding for eating disordered patients, such as body image cues or stimuli related to food deprivation and physical hyperactivity, showed several dysfunctions in ED patients. Moreover, very recently, it has been demonstrated that some of the biochemical homeostatic modulators of eating behavior are also implicated in the regulation of food-related and non-food-related reward, representing a possible link between the aberrant behaviors of ED subjects and their hypothesized deranged reward processes. In particular, changes in leptin and ghrelin occur in patients with anorexia or bulimia nervosa and have been suggested to represent not only homeostatic adaptations to an altered energy balance but to contribute also to the acquisition and/or maintenance of persistent starvation, binge eating and physical hyperactivity, which are potentially rewarding for ED patients. On the basis of such findings new pathogenetic models of EDs have been proposed, and these models may provide new theoretical basis for the development of innovative treatment strategies, either psychological and pharmacological, with the aim to improve the outcomes of so severe disabling disorders.

Contents

Abbreviations: ABA, activation-based anorexia; AN, anorexia nervosa; ANR, anorexia nervosa restrictive subtype; ANB, anorexia nervosa binge-purging subtype; ACC, anterior cingulated cortex; BN, bulimia nervosa; DLPFC, dorsolateral prefrontal cortex; ED, eating disorder; fMRI, functional magnetic resonance imaging; GM, grey matter; NAc, nucleus accumbens; OFC, orbitofrontal cortex; PFC, prefrontal cortex; TSST, Trier Social Stress Test; VTA, ventral tegmental area; WM, white matter.

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http://dx.doi.org/10.1016/j.pnpbp.2017.02.020
0278-5846/

1. Introduction

Anorexia nervosa (AN) and bulimia nervosa (BN) are complex psychiatric disorders of great importance for public health policies, since they are associated with a high burden of morbidity and mortality because of their severe medical and psychological consequences. They are characterized by aberrant eating behaviors aiming at maintaining a low body weight because of the patient's pathological fear of weight gain, associated with alterations in the perception of his/her own body shape. In AN, restriction of food intake and physical hyperactivity are the main aberrant behaviors through which a low body weight is attained, although in some cases binge eating followed by compensatory purging or non-purging behaviors also occurs. Therefore, two types of AN are identified: the AN restrictive subtype (ANR) and the AN binge-purging subtype (ANBP) (American Psyhiatric Association, 2013). BN, instead, is characterized by binge eating episodes followed by self-induced vomiting or by other behaviors, such as misuse of laxatives, diuretics or prolonged starvation, which aim to compensate for the excess of food ingested in order to prevent weight gain.

Although at present the etiopathogenesis of these eating disorders (EDs) is still unknown, it is widely acknowledged that biological, sociocultural and psychological factors likely influence their development, progression and outcome. Recently, the hypothesis that alterations in brain reward mechanisms might be involved in the pathophysiology of EDs has been put forward. Indeed, AN has long been conceptualized as a starvation-dependent syndrome developing because eating less food is perceived as rewarding initially, and is then maintained through conditioning to the situations providing reward (Bergh and Sodersten, 1996; Støving et al., 2009). Similarly, binge eating patients with BN usually report strong urges to eat with a sense of loss of control over their consummatory behavior before bingeing and a transient reduction of negative emotional states after bingeing. Therefore, it has been suggested that increased food-derived feelings of pleasure, which follow the consumption of large amounts of food during binge episodes, may help the patient to reduce his/her negative emotional states. Furthermore, a clinical key symptom of EDs is represented by anhedonia, that is the reduced patients' ability to experience reward. Therefore, in the last years, brain reward circuitry and mechanisms have been a major focus of research in the pathophysiology of EDs.

The main reward circuit in the brain includes the ventral tegmental area (VTA) whose dopaminergic neurons project to the nucleus accumbens (NAc), which is part of the ventral striatum (Fig. 1). Once the VTA is activated by environmental rewarding stimuli, dopamine is released in the NAc (Bromberg-Martin et al., 2010) and induces motivational processes, which lead to the consumption of reward (Volkow et al., 2008). Several other limbic regions receive projections from VTA, such as hypothalamus, amygdala, hippocampus, and cingulate gyrus (Fock and Khoo, 2013). The phasic release

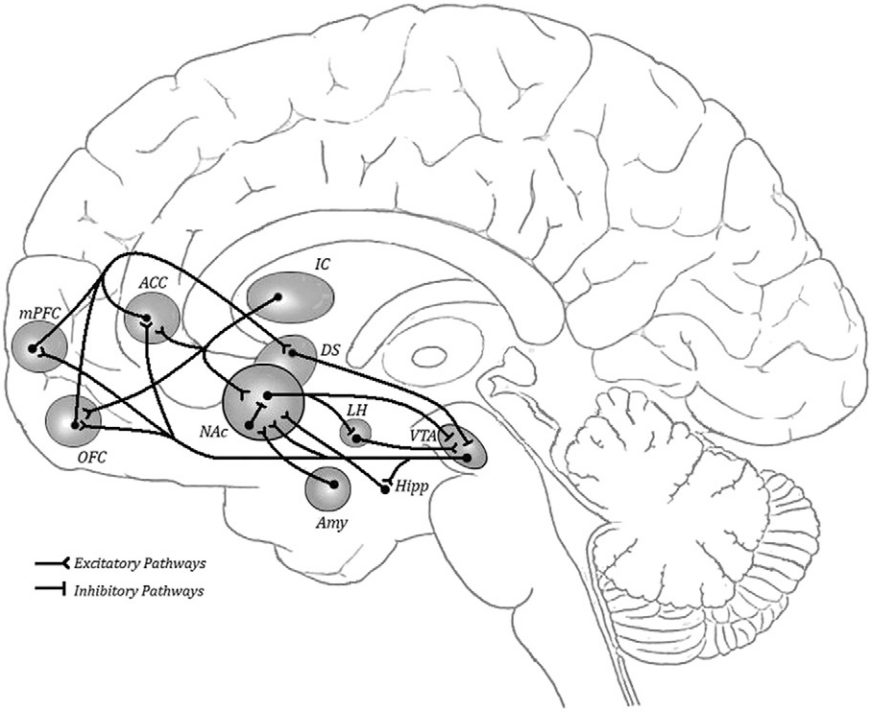

Fig. 1. Schematic representation of brain reward circuits. ACC anterior cingulated cortex; Amy amygdala; DS dorsal striatum; Hipp hippocampus; IC insular cortex; LH lateral hypothalamus; mPFC medial prefrontal cortex; NAc nucleus accumbens; OFC orbitofrontal cortex; VTA ventral tegmental area.