

Motivational/Emotional Systems in Eating Disorders

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Abstract

Eating disorders such as *anorexia nervosa* and *bulimia nervosa* still remain a malaise poorly understood in its etiology, and even less in its treatment. Affective neuroscience has shown that human personality is rooted in primary motivational/emotional systems that have been shaped along their own phylogenetic history. Eating disorders are increasingly recognized as an expression of the motivational/emotional systems involved in the dynamics of Sexual selection starting from adolescence. The latter pushes sexually mature individuals to compete for obtaining partners, and competition constitutes a vulnerability area for females affected by eating disorders. The intra-sexual competition hypothesis of eating disorders emphasises the importance of hormones and the links with dissociated functioning.

Keywords: Affective Neuroscience; Brain Emotional Systems; Eating Disorders; Dissociation; Social Competition

Introduction

Eating disorders, particularly anorexia nervosa and bulimia nervosa [1-3], are considered psychiatric disorders with multifactorial genesis, unknown etiology and rather strenuous clinical treatments. The prevalence of eating disorders in scientific literature doesn't turn out shared estimate due to the difficulty of standardizing the studies aimed at defining it [4]. The case frequency of anorexia nervosa is relatively low, ranging between 0.3% and 1% and 0.5% - 3.0% for bulimia nervosa [5,6] furthermore the average age of eating disorders onset turns out in the 14 and 19 years age bracket. The chances of anorexia nervosa cessation are estimated to be below 50% over a 10-year follow-up, while about 25% of patients there is no cessation, and mortality shows great variability, up to estimates of above 18%, one of the highest mortality rates among various psychiatric disorders [7,8]. Long-term bulimia nervosa cessation outcome is about 74% [8-10]. Eating disorders still remain a psychiatric pathology with a partly mysterious etiology. Consequently, the therapies implemented are affected by a high degree of empiricism/analysis/testing/assumption likewise by partially theoretical attempts at explanation. Yet, historically family-based approaches [317] have dominated interventions for adolescents whereas individual psychotherapy those for adults [11,12,303,326]. Real psychotherapeutic efficacy of treatments is difficult to be evaluated for eating disorders, especially for anorexia nervosa: "Despite this, no one treatment is considered superior, and all existing behavioral approaches leave a proportion of adults symptomatic or at a high risk of relapse" [303] and "However, a major limitation in AN research is the lack of untreated comparison

groups... Therefore, we do not know much about the "real efficacy of treatments". [12]. However, cognitive-behavioral therapy (CBT) is increasingly used for adolescents [13], while psychodynamic psychotherapies [14,15] seem useful for those patients who don't respond to brief treatments [16].

This difficulty in finding an effective psychotherapeutic intervention for eating disorders is largely connected, as mentioned above, to the still poor understanding of their etiology. Anorexia nervosa and bulimia nervosa, share some features which allow us to study their common etiology [17]. One feature involves that the eating disorders are more common among females than males. Other features that anorexia nervosa and bulimia nervosa share are both the concern for body shape and weight, the latter controlled through self/starvation, vomiting and exercise behaviors, and the self-esteem influenced by the fear of fatness and distorted body image [18,309,300]. Anorexia nervosa is characterized by a restriction of the introit of food and low weight, while bulimia nervosa by a compulsion behaviour for the intake of large quantities of food, followed by compensatory behaviours of vomiting, along with normal weight. In eating disorders there is a third category called either eating disorder not otherwise specified (EDNOS) in past editions of the DSM. This third eating disorders diagnostic category was developed to include those individuals who did not exactly meet the diagnostic criteria for anorexia nervosa or bulimia nervosa, even though they show eating behaviors that cause them clinically significant distress.

Eating disorders are serious mental illnesses characterized by massive dissociative states that does not allow the recognition of her own symptoms [19-21]. Consequently, this makes it a particularly favoured observatory for the study of states of consciousness and motivational/emotional systems, which highlight their presence in such symptoms (See in this regard H. Jackson, 1884, in Giacolini, 2022) [22,23]. Finally, eating disorders are an alimentary dysregulation that may appear in a more or less transitory way in numerous psychiatric disorders, from mood disorders, to anxiety disorders, personality disorders and psychosis [311]. Consequently, eating disorders turn out expressions of the functioning and evolution of the BrainMind [25].

The evolutionist point of view [26-28,307] and the study of motivational/emotional systems [25] are particularly rich in heuristic perspectives in the field of psychopathology and eating disorders studies [17,28]. For this reason, understanding eating disorders from the evolutionist point of view could allow to identify and to reconstruct their functional and adaptive necessity within the phylogenetic dynamics of brain/mind emotional systems. The latter have evolved in the mammal species to regulate the interaction among conspecifics, not only during the nursing period of the offspring but also subsequently in the interaction between adult individuals. Eating disorders significantly appear in adolescence [29,30] turning out a species-specific behavioral and emotional response to the new relational dynamics of this developmental stage. The latter concern the competitive interaction among sexually mature individuals [31], interaction regulated by some peculiar primary motivational/emotional systems [17,32,33].

The motivational/emotional systems are considered the biological roots of the human personality [34-36,328], and their functioning particularly happen in brain subcortical areas. This latter is one of reason of their functioning largely unconscious, as Freud already highlighted respect to sexual system [37]. In this paper it will be highlighted those motivational/emotional systems that, inside human personality, support intrasexual competition among sexually mature individuals within the framework of Sexual selection [31,32,38,39].

Now we would like to briefly reassume the aims of our study. The first one is to test the motivational/emotional systems in eating disorders patients in comparison with non affected ones. The second aim is to study the motivational/emotional systems that sustain the social competition and their connection with eating disorders the so called dominance and submission systems that were selected over species evolution [40,41]. Social competition is characterized by two behavioral and emotional systems, the one to achieve the dominance in the competition and the other the self-protective submission to show the recognition of one's inferiority in the struggle. The eating disorders could be understood like an automatic, outside of conscious control and then an involuntary Submissive behaviour

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for managing the social competition stress [320,321]. So, the eating disorders highlight an involuntary, dissociative and unconscious functioning. This latter can be shown applying the evolutionary Hughlings Jackson's dissolution hypothesis [22,24,332] to the dynamic of emotional/motivational systems in eating disorders. The third aim of our study is describing briefly both the endocrinological researches and neuroimaging studies on eating disorders.

Brain emotional systems and eating disorders

The historical merit of affective neuroscience [25] is to have the neuroscientific study of motivational/emotional systems re-proposed [42], that had been already identified and named like instincts by Charles Darwin (1809-1882) and Sigmund Freud (1856-1939) as the dynamic foundations of human emotional and mental activity.

Instincts and emotions had been central points of reference in the understanding of mental functioning [43]. Darwin's thought had a central influence in the evolution of psychiatry in the late nineteenth century, determining the development of a dynamic psychiatry focused on the recognition of instincts and emotions as aspects connected to the of psychopathology etiology [43,44,318]. Darwin proposed a bi-instinctual theory [45] centered on the struggle both for the individual's survival, natural selection [46] and for sexual reproduction called Sexual selection [31].

Freud made the Darwinian lesson his own, first as an evolutionary neurobiologist [47], then as a neurologist [48] and finally as a psychopathologist [49], contributing significantly to the development of the nascent dynamic psychiatry [50]. He developed a general theory of normal and pathological mental functioning centered, as it is well known, on instincts, primo movens of psychic functioning [51]. In the so-called first drive theory [45,51,52], mental functioning is the result of the conflictual interaction between sexual instinct and instincts of self-preservation, among which the aggressive instinct holds a particular position [53].

As is well known, the psychodynamic personality model developed by Freud is especially suited to the male gender (See Oedipus complex or Castration Anguish) and well represents an application of the Darwinian sexual selection [54]. Freud considered that sexuality could create other types of problems to the women, that is the anguish making mistakes, being reproached, losing love and the bond of belonging to one's family group, therefore the fear for their own self-preservation [37,313]. Freud in minute G writes: "The nutritional neurosis parallel to melancholia is anorexia. The famous anorexia nervosa of young girls seems to me (on careful observation) to be a melancholia where sexuality is undeveloped. The patient asserted that she had not eaten, simply because she had no appetite, and for no other reason. Loss of appetite-in sexual terms, loss of libido" (Freud, 1892) [55]. An extremely modern statement when compared with Affective Neuroscience propositions about depression as an expression of a massive depletion of the dopaminergic system that is SEEKING system [56]. It (depletion) inhibits the action of a person in the face of the threat or the loss of a bond, making it pass from the previous position of protest to the next one of despair and withdrawal [57]. The withdrawal, ethologically functional to the survival of individual animal not making itself visible to predators [58] and in the social competition like a submission behavior [59,60], in human species is equivalent of melancholia and the eating disorders could be considered as a behavioural manifestation of it [61].

So, the conflictual dynamics of sexual selection have been identified since the birth of evolutionism and dynamic psychiatry and even up to very recent times, especially in the male gender [62,63]. For some years, however, studies have increased that highlight how Sexual selection implies a stressful competitiveness even within the female gender in many animal species, including the human species [63,64]. So, these findings have provided a new heuristic basis for understanding of food disorders.

Brain emotional systems and dissociation

Eating disorders for long time have been included among the symptoms present in dissociative states [65-67] and dissociation has been a phenomenon that has attracted the interest of psychiatry since the beginning of its inception as a medical discipline. The first reference author that introduced a dissociation theory was undoubtedly the English neurologist John Hughlings Jackson (1835-1911). He described

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the development of the human nervous system as the result of the evolution of a hierarchical structure of three superimposed systems [22]. According to this principle, in the human brain architecture, the most evolved circuits of the nervous system inhibit and regulate the most primitive ones [22,68]. The most evolved of these systems is characterized by greater adaptability and learning capacity and corresponds to cortical functions, in particular the prefrontal cortex ones. The other two lower levels of the nervous system are characterized by fixed responses to environmental stimuli, reflex and instinctual responses. In case of an excessive stress load, this pyramidal organization can undergo "dissolution" [22], and the more recent circuits (cortical ones) cease their regulatory function and the older, more automatic systems intervene [22,69]. Jackson's evolutionary neurological model of dissolution particularly suits for explaining dissociation [23]. The latter turns out a manifestation of the disruption of the evolutionarily more recent brain functions, connected to the reflexive capacity, consciousness and working memory and the affirmation of the more automatic and instinctual lower systems, wired in the procedural memory of the species' evolution, less under voluntary check [23].

Finally, Jackson's theory of the brain tripartite hierarchical division have thereafter been sustained by later neurologists such as Paul McLean [70] and Jaak Panksepp [25,71], even though with their own specific neurological descriptions.

Structural dissociation of personality

A "theory of structural dissociation of personality" [67] has developed over the last years, whose central point is the dynamics of "action systems". These latter are synonyms of the emotional/motivational systems selected over mammals phylogeny for regulating the interactions with both the natural environment and among conspecifics [25,67]. The "action systems" are organized into two broad categories, those appointed to pushing the person into approaching the desired object and those appointed to moving away from a threatening object. These "action systems" are expressions of the two primitive ancestral tendencies of approaching and distancing [72-75] and they correspond to the motivazional/emotional systems described by Affective neuroscience [25,67]. These systems are named SEEKING, CARE, LUST, PLAY (the use of capital letters for primary emotional systems was proposed by Panksepp, 1998), that are sources of positive affects [25] which motivate the individual for approaching a desired object. Vice versa, the FEAR, RAGE, SADNESS systems, that are sources of negative affects [25], motivate the individual for defending and moving away (distancing) from a danger object. The integration of these two groups of motivational/emotional systems [76,77] can be prevented by subjective experiences when they exceed a certain threshold of stress (i.e. trauma) and so the cortical regulation weakens itself and the Dissolution [22] of the BrainMind organization allows the defensive motivational/emotional systems (FEAR, RAGE, SADNESS) to leader the human behaviour. This state of stress could be caused either by the environmental actions on the individual or by the human developmental stage of adolescence like a (Physiological) Developmental Trauma [78]. The latter refers to the peculiar functioning of motivational/emotional systems in adolescence species-specific human stage. This functioning, mostly in vulnerable adolescents, can gives rise to a massive activation of the distancing systems such as hypervigilance, flight, fight, freeze, and submission [67]. Hence the dissociative manifestations like, for example, both neurofunctional disorders (conversion hysteria) or eating disorders [331]. Anorexia nervosa would clearly show in the focal avoidance of food, completely devoid of a reasonable explanation, a behavior that indicates in the food an extremely dangerous threat that must be avoided. Similarly, bulimia nervosa manifests the person's desire for appropriating and ingesting food, which is immediately afterwards expelled because estimated dangerous by her. Why is it so? What could be the shared etiology? The next paragraph will deal with two motivational/emotional systems, still relatively little studied, that regulate the social competition and that could be considered as a possible cause of these psychopathologies. These two complementary systems are called dominance and submission [29,45,79] and later in the article the two ones will called dominance/submissive system in synthetic form. It's necessary to remember that dominance/ submission motivational/emotional system has been studied formerly like both agonistic behavior [80,309] and rank theory [81,82] too.

Social competition and eating disorders

Among the primary motivational/emotional systems [25,83], some of them have evolved electively to regulate the relationships between conspecifics, in particular in mammals (but also in various species of birds), therefore late in phylogenetic history. These are the

SADNESS system which organizes the alarm behaviors of the attachment system, the CARE system for the care of the offspring and the PLAY system [25] which regulates the relationships within the litter [84,85]. Two more archaic systems than the previous ones, the RAGE and the FEAR systems, had evolved for the organism defense. Over the vertebrate phylogenesis these two systems have been co-opted for giving rise to a new complex dominance/submission motivational/emotional system. This latter regulates the intraspecific interactions between sexually mature individuals, in order to have access to food and sexual resources. These conflictual interactions are expression of sexual selection [31,86,87]. During the activation of the dominance/submission system, the RAGE system pushes the individual to competition. Conversely, the loser in the confrontation, by activating the FEAR system, runs away and so inhibits the aggression in the contender. Among social mammals living in groups, the flight is replaced by the more complex behaviors of submission [45,81,83]. The loser manifests the recognition of the opponent's superiority in the competitive challenge, displaying behaviors of pacification i.e. Submission behaviors, so the winner tolerates the closeness of the loser yet in a hierarchically subordinate position. As it is known there are species-specific pacification behaviors from a loser towards a winner, such as behaving like puppies of their own species, showing behavior of sexual offering typical of females etc. [319]. The evolution of submission behaviors, replacing simple escape, have allowed group life and the coexistence of the dominant and the defeated, through the establishment of a hierarchy of rank [81,82,84]. This latter not only regulates accessing to food and sexual resources but even it allows individual to remain within the group one belongs to and therefore taking advantage of the proximity to one's own conspecifics.

Social competition among females

Neurobiological research has highlighted that, in many species, individuals of lower ranks (i.e. submissive ones) are placed right on the group borders and they shows permanently stress, that is a persistent alarm [85-87]. These behaviors, as mentioned above, have been studied primarily in competitions among males in most mammal species. In recent years, interest in the study of females social competition and rank issues has more and more increased [40,88-101]. Researches indicate that competition for dominance also occurs among the females. The function of the dominance position in female mammals seems above all regulates priority access to food resources, closely linked to the acquisition of greater energy resources for mating and breeding of offspring [102,103]. This function of dominance position is particularly visible during environmental food famine [103-105]. When food is scarce the dominant females have the priority over the access of food resources and so they have evident better nutrition in comparison to the lower ones. Therefore, the dominant females have a greater capacity and frequency of mating, of fecundation and of raising their own offspring faster. In these situations, the position of rank and therefore the access to scarce food resources, determines a severe differentiation in the reproductive possibilities, almost exclusively expressed by the dominant females. The etiological research show, therefore, that the mammal females competition for social rank is not only strictly connected to the food dimension but has a similar importance to that for the male gender [94,100]. From a neurobiological point of view this implies the presence in females of an dominance/submissive motivational system similar to that present in males [33,106,107,300]. Studies related to the dynamics of androgens in females have highlighted the same dynamics that exist in males, i.e. commensurate increased aggression, dominance and sexual desire to the increase of androgens [33,106,108-110]. The existence of analogous androgen receptors in the female brains have also been proven [111-113], even though it should be remembered that testosterone production in females is much lower than in males [114]. Later in this article we will return on the function of hormones in the dynamics of eating disorders.

At the same time, females are also vulnerable to social defeat stress. The social defeat paradigm [115] derives from animal studies, such as those for submission behavior, to analyze the behavioral and physiological responses of the loser in an intraspecies competition [116]. The social defeat describes the experience of defeat arise in competition in everyday life, from loss or a reduction in one's perceived ability to compete for social place, for friends, lovers etc. So, the individual feels herself inferior to others because of self-judged inadequate personal qualities, often linked to unrealistic goals or standards and to harsh internal self-criticism [117,118]. The experience of social defeat activates submission behaviors aimed at managing the state of defeat and defuse the aggressiveness of the contender in the paradigm of

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social competition [119]. The females social defeat vulnerability [98,120] highlights the complex problem about how much it is due either to the genetic and epigenetic dimension [121-123] or to transgenerational transmission [124-126], particularly through observational learning of the parents [57,127]. This vulnerability implies an increased tendency to a negative comparison [314] towards other females and an equally involuntary tendency to activate submission behavior, that is called involuntary subordination [83,128,315], characterized by anxiety and depression [129,130]. Characteristic of submission behavior, as indicated above for males, is publicly making recognition of one's inferiority manifest to other members of the social group, even through holding back herself from food (and sexual) resources. In the phylogenetic evolution of female submission behavior [131,132], the control of food motivation has been a salient behavior [133-135] in order to postpone satisfaction, for no rekindling competition, that is assessed by the individual defeated as dangerous [17,135-137,304]. Stress induced by social defeat and submission behavior expresses a psycho-physical state which in turn could contribute to the onset of eating disorders [137-140], whose consequences are seen in the lack of appetite or hyperphagia and vomiting [135,141,142]. The emotion connected with the attempt to avoid social defeat stress is the shame [143-146], an expression of inferiority and then a submission behavior. In evolutionary epistemology, shame is the emotion that inhibits the action of the individual who evaluates oneself inferior [147], thus curbing the subject's exposure to a ruinous conflict with conspecifics evaluated as more qualified and superior. In eating disorders, shame activates food restriction [148], inhibiting one's social assertiveness towards food perceived as a dangerous object. In anorexia nervosa, shame frequently is replaced by the emotion of pride [145,146] when the subject reaches a desired restrictive goal. The vulnerability to social competition expressed by eating disorders raises a further question, to what extent its being a specific phase connected to the sexual development is also an expression of a previous vulnerability in the motivational/emotional Attachment system [149-151]. Eating disorders make their classic appearance in adolescence [124], when sexual development determines a decrease in the primacy of the parental Attachment system in the regulation of emotional states and pushes subjects to compete within Sexual selection [152]. The alarm caused by this new developmental stage can gives rise to, in vulnerable subjects, Involuntary Defeat Strategy [153,154] even called involuntary subordinate strategy [59] or Involuntary subordination [83,128], all synonyms for describing an automatic defense reaction [155]. This latter, such as indicated above, causes the girls' difficulty in transferring emotionally significant ties from parental figures to new partners [156,157], whom they should conquer in the dynamics of Sexual selection.

The dynamics of hormones in eating disorders

Hormones are evolutionarily quite conservative, many of them with similar chemical structures across species [159], a window of particular importance for studying the evolution of motivated behaviours. The hormones are subordinate traits, positioned to mediate integrated responses to environmental adaptation, then both to natural and sexual selection [160]. Evolutionary neuroendocrinology is a relatively recent point of view in the field of hormone studies, but of particular importance to highlight how single hormones can determine different phenotypic expressions from the same underlying genetic basis [161].

The eating disorders are linked to a very important, multiple endocrine alterations [162]. Many hormones undergo alteration, especially in anorexia nervosa, such as increase of secretion of cortisol and growth hormone (GH), whereas there is a decrease of leptin, sex hormones and thyroid hormone [163]. In anorexia nervosa the hypersecretion of cortisol is linked to self/starvation and to motor activity and this latter increase the opioid dynamic. Both opioid and ACTH derived from the same prohormone pro-opiomelanocortin (POMC) [162,164].

Yet some hormone dynamics are involved as causes of vulnerability in eating disorders, and they highlight some exciting links with the social competition hypothesis. About this latter the dual hormone hypothesis [165,306] has underlined that motivation for dominance status correlates to high testosterone and low cortisol. When there is the co-presence of high testosterone and high cortisol, in this case cortisol would reduce the testosterone effect [166].

The dual hormone hypothesis has had an interesting application which concerns eating disorders in the studies related to the general strain theory (GST). This theory [167,168], highlights the tension in the individual due to the impossibility of achieving desired objectives,

especially in relation to one's status or due to the perception of being treated with hostility. This state of stress causes negative emotions, such as a sense of defeat, fear, depression, anger, for resolving which, in the absence of positive and socially shared solutions, one can resort to unsuitable and transgressive behaviors. This particularly in the developmental phase of adolescence. GST studies have shown a significant difference in the strain management between males and females. The former, if positive and shared management of the causes of stress are not possible, tend to have aggressive and markedly deviant behaviors, while the latter are more prone to depression and selfdestructive behaviors, such as self-harm and eating disorders, the latter are considered as analogous self-harming behaviors [169-171]. Furthermore, females would be much more vulnerable to the experience of strain and to the consequent depression that is also activated because of aggressive reactions, with a sense of guilt and inadequacy. The difference between males and females in the management of the strain effects has been connected to the dynamics of the dual hormone hypothesis [172]. This study highlighted how in males the testosterone/cortisol ratio, due to the greater presence of the former, favors the tendency towards externalizing behaviors, as aggression, while in females, where testosterone production is massively lower, the ratio between the first and the second favors internalizing behaviors such as depression [172,324]. Regardless of gender differences, individuals with low testosterone and high cortisol would be more prone to internalizing behaviors such as depression, anxiety, avoidance, self-harm and eating disorders [172], behaviors that can be classified as submission behaviors [173], while high testosterone and low cortisol favor externalizing behaviors [174]. The internalizing behaviors, more present in females, can also be associated with their predisposition to caring and nurturing which protects them from more aggressive or criminal behaviors [170] through the production of the hormone oxytocin [175,176].

The study of sex hormones has highlighted their function both in protecting against eating disorders and in promoting them. The dynamics of testosterone has shown that its production increases in the presence of threats to one's status, therefore it is sensitive to threats to the social self [177]. In females faced with any threats there is a greater production of testosterone than in males, probably because in females this hormone is mainly of adrenal origin and therefore more sensitive to stress dynamics [177,178]. The same seems to occur in males in the developmental stage referred to as adrenarche [179]. In this stage either males or females have significant production of adrenal-derived testosterone and this correlates significantly with an increase in stage-specific genetic vulnerability to eating disorders in males [180,329] but even females reported greater body dissatisfaction [181]. Testosterone has a protective function against binge eating and bulimia in either males or females, but too high testosterone exposes females to the risk of anorexia [182]. As known males experiencing substantially higher levels of the testicular hormone testosterone perinatally in comparison than females. So, the formers' central nervous system (CNS) is more responsive to androgens later in development, while in the females a relative lack of perinatal testosterone organizes their CNS to be more responsive later in development to estrogen and progesterone [182]. While in males high, testosterone production is protective against eating disorders, in females this function is performed above all by estrogens, in particular by estradiol, while progesterone would have the opposite effect [182]. Progesterone, appear to significantly affect body image concern in relation to social stimuli, such as the expected judgment of peers to conform to [183]. Studies that interconnect resting state neuroimaging with hormonal dynamics [184] have highlighted that the premenstrual phase characterized by an increase in progesterone production determines an increase in connectivity, a window of vulnerability for depressive problems and emotional eating [184,185]. In the middle luteal phase, where the production of progesterone is greater, the response of the amygdala to stress increases and the connectivity between it and areas of the default mode network (DMN) increases, causing a vulnerability to depression and to memory for negative contents [186]. The function of DMN appears to be to monitor and manage the attention directed to one's self and self-referential processing processes. The other resting state network called Salience network seems to managing stimuli from the outside world and therefore particularly activated in situations that give rise to post traumatic stress disorders (PTSD). In this case, the connectivity inside DMN decreases. The luteal phase in which progesterone production increases seems to favor overlap between the DMN and the salience network in various brain regions, in particular with the amygdala [186] resulting in a greater ability to memorize unpleasant events and easier to retrieve them, leading to negative affective experiences.

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Steroid hormones have an important target in the brain, influencing both the development and plasticity of the brain and the creation of neural networks, starting from prenatal periods. These circuits partially remain dormant until the pubertal hormonal development determines their full activation giving rise to the related behaviors [187,188]. The organizational-activational hypothesis [187,189] has shown that the organizational function of hormones on the brain continues even during puberty and adolescence and that social experience modulates the interaction between steroids and the brain of adolescents by acting on the emotional and the behavioral development [190,191]. One of the functions of hormones is therefore to favor connections for the formation of networks in the brain and to favor or limit their functionality [192]. In the formation of networks particular importance has testosterone [193] on neurite outgrowth, number of synapses, dendrites [194] and myelination. Pubescent females with a greater production of testosterone and of estradiol have an increase in white matter in networks involved in cognitive control, response inhibition and emotion regulation [196-198]. Higher testosterone and white matter production in females also correlates with higher vulnerability to depression, anxiety, and substance use [199] and eating disorders [201]. Other studies show that in eating disorders are the DMN (Default mode network) related to self-reflective cognition (Self-focused and body-focused thoughts), the ECN (Executive control network) related to cognitive and executive functions, BGN (Basal ganglia network) [202] and SN (Salience network), which is involved in the evaluation of internal and external stimuli to support behavior choice [203].

The study of the relationship between hormones and resting state connectivity has highlighted the contribution of steroid hormones to the modulation of the brain networks. The administration of exogenous testosterone has shown that it affects the reduction of the connections between the amygdala and the DMN, reducing the cortical regulation on the amygdala, both in males [204] and in females [205] and favoring the subcortical connections between the amygdala and thalamus [206]. The exposure to high levels of testosterone in the intrauterine phase has shown a significant positive correlation with the onset of many psychopathologies, as already mentioned above, anorexia behaviors in females [207], autistic syndrome in males [208,209] and psychotic states [210].

Closely related to these psychopathologies is the effect of testosterone in implementing the dopaminergic system response, particularly during adolescence, including the pleasure of physical exercise so present in eating disorders [211-213]. The study of the dopaminergic system has highlighted the positive correlation between the dopaminergic system and the onset and dynamics of both psychosis [214] and eating disorders [215-217,316]. In recent years there has been growing empirical evidence relating to the comorbid associations between psychosis and eating disorders, in particular anorexia nervosa, in which symptoms characterizing psychotic functioning are traceable and conversely eating disorders-related features in psychosis [218]. The psychotic functionings in eating disorders can be distortions of body image, usually associated with idiosyncratic convictions on food effects on body and overvalued ideas to delusion-like beliefs, as well as poor insight about one's symptoms and one's ideas, scarcely susceptible to being confronted with conflicting evidence [219].

Among the non-sexual hormones, cortisol, as already considered above, has an important function in various psychopathologies as eating disorders, mood disorders, psychosis and addictions. In adolescence, parallel to the increase in the activity of the dopaminergic system connected to the production of testosterone [213], there is a proliferation of glucocorticoid receptors (GR) in the dopaminergic system, especially in the prefrontal cortical areas [213]. This last aspect highlights the vulnerability of adolescents to social stress. n adolescence the gonadal steroids, testosterone and estrogens, influence the proliferation of oxytocin receptors in the various limbic structures, including the amygdala and nucleus accumbens [221]. This phenomenon in adolescence seems increasing salience for social emotional stimuli and the awareness of the opinion of others and self-awareness [221]. In eating disorders the pathogenic trigger is frequently connected to negative social expectation, which activates the dopaminergic system towards the desired goal to avoid [222], that is avoiding the negative self-image through self-starvation and massive physical exercise, as in anorexia, or through food intake, as in bulimia, for reducing a negative emotional state. Therefore eating disorders, as addictions, seem expressing negative emotional states

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conceptualized as anhedonia [224] and from which the pathological behaviors aimed at avoiding this mental state in order to maintain the dopaminergic system activation [225,226,304,305]. The consolidation of abnormal forced food behaviors seems connected to an initial hyperactivation of the dopaminergic system, solicited by the social targets and behaviors considered above, which progressively determines an adaptation of the dopaminergic system with a reduction in dopamine release, as it is more evident in addictions [215]. The reduction of dopamine release in eating disorders seems to be closely connected to the chronic activation of HPA prompted by social stress, persistent caloric restriction and low body weight. Chronic stress decreases cortisol production [227] which in turn determines a reduction in activity of the dopaminergic system, which determines in the subject malaise and a forced drive to perpetuate behaviors aimed at increasing the release of dopamine [215]. Anhedonia in its meaning of social anhedonia, is characterized by the inability to find pleasure from social engagement [228,229]. This vulnerability is present in many psychopathologies, psychosis, autism, depression, eating disorders. In these latter it has highlighted that the dysregulation of the dopaminergic system is not confined to eating behavior or dysmorphobia but it is strongly connected to social interactions [228]. Social anhedonia is, therefore, an important transdiagnostic dimension underlying many psychiatric disorders and has been linked to social defeat [230,231]. This latter, as explained above, is a mental state in which the individual experiences the conviction of being unable to achieve one's own goal in relational dimension, hence the sense of defeat [230]. It should be remembered that anhedonia is one of the main negative symptoms of schizophrenic psychosis [232,233], in which there is a depletion of the dopaminergic system, unlike the positive symptoms which are connected to an hyperactivation of the dopaminergic system [234].

Eating disorders in neuroimaging

The neuroimaging studies related to patients with eating disorders are few but increasingly, even though the findings are still not so clear and sometimes contradictory [235,236]. The neuroimaging studies must manage multiple intercurrent variables, from the small study samples to the overlapping of the neural networks, hormonal status, medication use, comorbidity [216,236]. Neuroimaging studies in eating disorders cover three broad areas of functioning: cognitive control, reward processing and emotional processing, that interact with each other [236]. The neuroanatomy of the neural networks that characterize these three dominions have overlapping across circuits [237,238]. To date most neuroimaging researches have focused on anorexia nervosa, with less data available for bulimia nervosa [236,302]. Cognitive control in anorexia nervosa shows a great visible control in food restriction and perfectionism [237,239], whereas bulimia nervosa shows greater impulsiveness and loss of control over eating [237,240]. Some brain regions involved in cognitive control are the prefrontal cortex (PFC), the orbitofrontal cortex (OFC), the anterior cingulate cortex (ACC), the parietal cortex [236,241]. The reward processing poses difficulties to neuroimaging studies due to different results for different stimuli utilizing in the researches on eating disorders [242,243]. Hence there are conflicting data about whether anorexia nervosa is characterized by a lower reactivity of the reward system compared to a greater reactivity of bulimia nervosa [244-246]. The neural networks of reward system include the ventral and dorsal striatum, the amygdala, the parietal cortex, insula, PFC, OFC, ACC [236,247,248]. Among the reward system studies interestingly are those on habit learning in anorexia nervosa. In this latter the food restriction behavior repeated over time may determine the passage of control from the ventral striatum to the dorsal striatum and then the development of an actual ritual behavior [236,249,250]. Finally, neuroimaging studies of primary emotional systems [25,251] highlight specific challenges to researchers [252,253]. One of these is connected to subcortical regions that regulate the emotional systems, which present greater difficulties in visualization than the cortical cognitive control ones. The latter are characterized by larger cortical networks with rapidly firing cells in comparison with smaller subcortical regions with slower firing neurons linked to unconditional emotional behaviors [254-256,323]. The neuroimaging studies of emotional systems in eating disorders mainly concern negative affects that include anxiety, sadness, fear, anger, guilt, shame [236,257,258]. SADNESS, ANGER, FEAR are few of the primary emotional systems (Unconditioned Emotional Response systems [25,251]. The latter of the three systems is the root of submissive behaviour, whereas the other two ones are involved in the complementary dominance behaviour [259-266]. The FEAR system involves some circuits, extended amygdala, hypothalamus, periaqueductal gray (PAG),

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ventral pontine tegmentum, ventral and dorsal medulla, ACC [258,267-272]. In anorexia nervosa the food-cues increase activation in the amygdala and fearful responses together with a simultaneous decrease in the activation of the reward regions [236,273-275]. Usually the food-related stimuli activate the reward regions in bulimia nervosa studies even though there are researches that highlight fear and disgust in front of those stimuli ones [329], with hypofunctioning of the ACC (Anterior cingulate cortex) similar to what was seen in the anorexia nervosa studies [236,276]. The emotional FEAR system is also closely related to the SEEKING system, i.e. dopaminergic system. The former powerfully starts up the latter [222]. The interaction between these two primary emotional systems activate the ventral striatum and, if repeated over time, as already above highlighted, it may increase the passage of control from the former to the dorsal striatum, causing the consolidation of the response as a habit [223,277,278]. Stress is generally connected to activation of negative emotions in eating disorders even though neuroimaging studies showed bit murky data [236,280-283].

Conclusion

The present work is in line with the evolutionary literature [284-286], that points out intra-sexual competition hypothesis one of the ultimate causes [268] of eating disorders. Both the reproductive suppression hypothesis model [289,290] and the sexual competition hypothesis for eating disorders (SCH) [17,32], recognize these symptomatologies as a significant vulnerability to social competition [28]. Specifically, the eating disorders could be considered the defensive consequence of sexual maturation that pushes the subject into the competition for sexual selection [31], in which the desire for mating and the activation of motivational/emotional systems of dominance/ submission are simultaneously present [45,79,230]. Both LUST system and dominance/submission system push the subjects to a massive social comparison [33,291,292,308] which seems provoking a self-judgment of inferiority in eating disorder patients [33,293,294]. Eating disorders show the difficulty the young girls in managing one's functioning in the new context determined by sexual maturation. This latter pushes the adolescents out of the protective environment of the attachment system connected to the parents of one's childhood. In the human species the LUST system pushes the adolescents to establish new attachment relationship [295,296,310,312,325]. The girls with eating disorders seem showing a peculiar difficulty to manage the dominance/submission system, which doesn't allow them to direct LUST system [25] and then to set up new attachment relationships. This type of functioning could determine the perverse fear circle of sexual competition. So, the withdrawal from food could be explained as a pacification/submissive signal that shows the withdrawal from sexual competition for mating [85,86]. At the same time, food dysregulation could be understood as a request of protective attachment [297] addressed to the adult group. In this perspective, eating disorders could be explained as a dissociated expression of some motivational/emotional systems, LUST, dominance/submission and attachment ones [322], each one functioning in a basically subcortical, implicit and automatic way.

Finally, it will be interesting to study in a next research the comorbidity between eating disorders, anxiety and depression that for a long time has been highlighted [61,298]. Comparative psychology studies have shown that separation from one's conspecifics, a social isolation, is a powerful activator of depression-like modalities in humans, as well as submissive behavior, where food restriction and weight decrease are involved [136,299].

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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