

MOOD DISORDERS, NUTRITION, AND CRAVING

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Abstract

Objectives: *The relationship between food intake alterations and mood disorders is a well-known phenomenon for various clinicians. However, these phenomena have been scarcely studied to date. The methods of evaluation of craving are diverse, generating heterogeneous and superficial findings. A more refined analysis of the phenomenology of craving and the various relationships between nutrition and mood disorders, specifically Bipolar Disorder (BPD), are the objectives of the present review.*

Method: *A narrative review was carried out through a non-systematic search of the literature through the MEDLINE database, using MeSH terms.*

Results: *The results in this area to date are scarce and diverse. We evaluated the evidence to date about the bidirectional relationship between BPD and nutrition, and Eating Disorders (ED), specifically, Binge Eating Disorder (BEA). On the other hand, the literature was reviewed in terms of understanding the concept of craving for carbohydrates, its neurobiology, and its relationships with mood disorders, specifically BPD.*

Conclusions: *Despite being concepts and relationships long-known by clinicians dedicated to mood disorders, literature and research was quite limited in relation to this. Independent academic efforts remain pending to continue developing in the understanding of the intimate mechanisms of these disorders, their clinical phenomena and diverse relationships, considering the important implications that they may have on the diagnosis, evolution and therapies of patients.*

INTRODUCTION

The presence of changes or variations from regular food intake, or inherent to eating disorders, is a well-known phenomenon for clinicians who typically evaluate patients with varying types of mood disorders. Changes in terms of an increase or decrease in appetite, day-to-day fluctuations in appetite, the appearance of what patients call “anxiety,” an uncontrollable desire at times to consume a specific type of food, changes in weight, the emergence of eating pattern changes of a restrictive or bulimic type in the prodromes of mood disorders, and the presence of night-binging

disorder or night-eating syndrome, are all symptomatic profiles of disturbances in food intake during the emergence of mood disorder phases with which experienced clinicians are greatly familiar, but which have not necessarily been precisely semiologically captured in the scales or texts, and, thus, neither in the field of research. This review focuses on discovering the problem and analyzing the scarce literature on the issue.

“Craving” for food is defined as a motivational state in which an individual feels the need to seek out and ingest a specific food

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(1). This phenomenon differs from the concept of hunger in that the intensity of the desire is greater in the craving, and there is also specificity for a certain type of food (2). Although this definition is quite specific, in the literature there are difficulties surrounding the objective assessment of craving. Attempts to assess craving have been made in many different, and at times dissimilar, ways, from self-assessment scales of craving to the measurement of the amount of food consumption, the speed of this consumption, and even psychophysiological measures. This has produced heterogeneity in the findings of published studies, as well as difficulties when making comparisons. In addition, the first studies conducted presented hypothetical and theoretical conclusions related to the concept of craving, without any empirical support (3). In general terms, there is no precise and suitable phenomenological description of craving in the literature; therefore, the majority of studies include a heterogeneous population of patients with limited assessment of the patterns and characteristics of the craving, such as for example the presence or lack thereof of a circadian profile, association or not with a stressor event, the type of food for which the craving emerges (carbohydrates, proteins, fats, and others), and whether the symptom decreases with intake of the specific food.

Thus, for this review, we have proposed the following phenomenological distinctions based on epidemiology and on recent neurobiological findings: craving in bipolar disorder, craving associated with anxiety, and craving associated with obesity.

METHODOLOGY

In November 2018, a search was conducted in the PubMed electronic database using the following MeSH concept search strategy: "Bipolar Disorder" OR "Bipolar and Related Disorder" OR "Mood Disorders" AND "Binge-eating Disorder" OR "Dietary Carbohydrates" OR "Night Eating Syndrome" OR "Feeding Behavior." References from the selected articles were re-

viewed below. A total of 232,968 articles were found with this method, including articles written in English or Spanish. Filters were then used, including the following types of studies: "Case Reports," "Randomized Controlled Trial," "Observational Study," "Review," "Systematic Reviews," and "Meta-Analysis." 29,816 articles were selected, of which 48 studies, which focused on the objectives of the review, were chosen and reviewed.

RESULTS

Bipolarity and Nutrition

Throughout life, various nutritional and food regimen alterations can be associated with multiple mental health aspects and disorders. In this regard, there is increasingly more evidence of a bidirectional relationship between nutrition and mood disorders. This is even more apparent in the adolescent population where unhealthy eating behaviors have been associated with depressive symptomatology, anxiety, substance use disorder, and suicidality. Moreover, the evidence pertaining to nutrition and Bipolar Disorder, specifically, is limited and not very consistent, which is worrisome considering the emerging evidence surrounding how patients with a bipolar disorder diagnosis could present worse eating habits than the general population, which, in addition to the challenges in adopting healthy habits, has been insufficient in itself for explaining the high incidence of Metabolic Syndrome (MS) in this population group. In this vein, Bly et al. did not find significant differences in diet and physical activity between bipolar patients with or without MS (5). Despite this, the presence of multidisciplinary approaches focused on nutritional management and physical exercise have indeed been successful in bringing about better final results in patients with bipolarity, considering metabolic aspects as independent prognostic factors for individuals with BPD (6,7).

In a post-hoc analysis of the BRIDGE-II-Mix (9) study for the assessment of mixed states in patients with a Major De-

pressive Episode (MDE), Petri et al. (8) observed that obesity in patients with MDE was linked to higher rates of bipolar spectrum disorders, suggesting even the possibility of considering obesity as a potential marker of bipolarity. Moreover, individuals with major depression and obesity also had a greater probability of having other factors associated with bipolarity (such as a greater number of previous episodes or atypical depressive characteristics). The rates of bipolar spectrum diagnosis were higher in adults with major depression with obesity versus adults with major depression without associated obesity.

Conversely, individuals with BPD have a significantly higher risk of suffering from diseases related to obesity; specifically in relation to alterations in eating patterns in patients with BPD, Dalkner et al. (10) observed in a cohort of 135 bipolar euthymic individuals that high levels of carbohydrate craving was positively correlated with levels of Kynurenine and with the Kynurenine/Tryptophan ratio (a finding found in various inflammatory and neuro-psychiatric diseases), also concluding that overweight and/or obese individuals with BPD demonstrate an increase in the conduction of Tryptophan via the Kynurenine pathways, which are mediated by immune-inflammatory activity and stress. The correlation between the increase in Kynurenine and the craving, particularly for carbohydrates, probably indicates a regulatory deficit in the maintenance of chronic inflammatory processes in obesity and in BPD. As such, the craving could have clinical importance in the treatment of metabolic disorders in BPD, even though it may not necessarily be associated with anthropometric measures of obesity. Rather, the desire for food is correlated with blood metabolic parameters (triglycerides, high-density lipids (HDLs)), and an increase in the activation of the Kynurenine pathway, which are related to greater affective symptomatology and the development of cardiovascular diseases (10-11).

Bipolar disease generally starts at an early age; therefore, patients may be even more affected by aspects involving poor

nutrition over the long term. Furthermore, it has been seen that young patients with BPD present deficiencies of certain nutrients that could have a protective role in long-term mood alterations, such as vitamin C, magnesium, and zinc (12), which could be in addition to the high association between BPD and diets rich in glycemic load and processed foods, which, in turn, would be associated with greater risk of developing BPD in the future, particularly in women (13, 14).

Bipolar Disorder and Eating Disorders

There is high comorbidity between BPD and various Eating Disorders, such as Binge Eating Disorders, Anorexia Nervosa (AN), and Bulimia (BN); moreover, the prevalence of Eating Disorders that do not meet the formal criteria for these three entities (characterized as Non-Specified Eating Disorders) or within the subthreshold of the Eating Disorder spectrum is considerably higher in patients with BPD in comparison with the general population (between 3.6% to 10%). A strong association between BN, Bipolar II Disorder, and “soft” bipolar spectrum has been found in research in specific clinical sub-groups (15). Current evidence is significant in terms of the relationship of Binge Eating Disorders and “emotional eating” with BPD (16). Thiebaut et al. (17) carried out a systematic review of the articles, estimating the prevalence of BPD in eating disorders, and vice versa. In patients with BPD, 0.6% to 33.3% were found to have eating disorders. On the other hand, in patients with eating disorders, 0 to 35.8% of patients presented BPD. The association was greater for purging type Anorexia Nervosa and for Bulimia or Binge Eating Disorder, with comorbidity being more frequent in patients with early-onset BPD. Statistical significance was not observed regarding the sub-type of BPD.

There could be various reasons to examine the comorbidity between eating disorders and BPD; first, that these eating disorders would probably require a specific, pharmacological, or psycho-therapeutic treatment; second, if the prevalence of eating disorders in patients with BPD is greater

ter than expected, a specific evaluation becomes necessary, or vice versa (evaluate mood symptoms in patients with eating disorders); lastly, this comorbidity analysis may enable greater physiological understanding of both entities, especially in the affective components of instability and impulsivity which are common to them (18).

In population studies, in a survey of 2,548 individuals between 14 and 25 years, Wittchen et al. found that 9% met DSM-IV criteria for Hypomania or Major Depressive Disorder (MDD), and 8% presented a life history of eating disorders; also, the risks of suffering from eating disorders were significantly greater in individuals with Hypomania or MDD, more than in those with mania, compared with the general population (19). In another study of 810 women, Lewinsohn et al. found that including sub-clinical BPD criteria, comorbidity increases with complete or partial presentations of eating disorder syndromes (20). It seems apparent in the literature that the comorbidity of eating disorders and Bipolar Spectrum Disorder is high, even more so in adolescent women. Upon systematizing information, differing results are found regarding prevalence (primarily due to methodological challenges); however, prevalence of BPD in Eating Disorders throughout life is 7.25%, and is consistently higher than in the general population (21).

Patients with this comorbidity present a worse prognosis, they tend to develop BPD with an earlier onset, and with greater clinical severity (22), and they present some common clinical patterns, such as impulsivity and emotional deregulation. Furthermore, obese bipolar patients have higher risk of binge-eating disorder psychopathology, presenting loss of control of food intake (over compensatory behaviors). When both cases co-exist, there is also an association between atypical depression symptoms and binge-eating disorder. These findings are relevant because they dismiss the observation that these eating disorders may be due to consequences from the use of psychiatric drugs that cause an increase in appetite and weight, such as lithium, valproate, or antipsychotics, and are generally

characteristics of the population sub-group in question (24).

Overall, there appears to be a sequence in the onset of both disorders when they are co-morbid, with onset of the mood symptoms before the eating disorder. In this regard, a causal hypothesis could be that the occurrence of the alterations in eating could be secondary to the mood disorder, and that they could be a maladaptive response to mood instability and intensity of symptoms (25). From another perspective, there is abundant evidence on how an unbalanced diet affects the development of BPD, aggravating the mood symptomatology, which the bidirectionality of the relationship between nutrition and BPD could corroborate.

Bipolar Disorder (BPD) and Binge Eating Disorder (BED)

BED went from being an unrecognized eating disorder prior to DSM-5 to currently becoming the most common eating disorder in the United States (26). For the definition of BED, emphasis has been placed on the excessive intake of food associated with mental ailment in relation to this intake. In this definition, there is no reference to the specificity of the intake, whether it is food rich in fat, protein, or carbohydrates. Therefore, with this definition it is not possible to recognize patients with specific cravings within binge eating disorders. It is also not specified whether the associated ailment is prior or subsequent to the binge, thereby including dissimilar cognitive patterns in the interaction with the disturbed food intake pattern. Even so, there is vast evidence that BPD and MDD diagnoses are the most common in patients with BED (27). Specifically in relation to BED, when it is significantly associated with mood disorders, the burden of the disease increases considerably, presenting greater association with anxiety disorders, substance use disorders, maladaptive personality traits, and metabolic disorders (28). Furthermore, patients with BPD could be particularly affected if they have comorbidity with BED given they present a higher rate of suicidality, psychosis, comorbidity with anxiety

disorders and mood instability. Similarly, obese patients with BPD are more likely to have BED than those who are not obese (15.3% versus 5.1%), and this is also correlated with an older patient profile, female, with greater prevalence of suicidality and comorbidity with medical pathology (29). Boulanger et al. (30) analyzed a French cohort of 145 patients with BPD, in which 18.6% of the patients met the criteria for the binge eating behavior. Higher levels of anxiety and emotional reactivity were observed in these patients, considering these aspects as important factors of vulnerability shared between BPD and BED.

Carbohydrate Craving

Within the description of craving, it is appropriate to differentiate whether or not there is a type of food tied to the craving that is rich in fat, protein, or carbohydrates. Carbohydrate craving syndrome has been tied in the literature to dysphoric mood states as a type of form of self-medication (30). As such, the following criteria have been able to be operationalized (31):

Criteria for Carbohydrate Craving Syndrome:

1. Presence of a craving for sweets or food prepared from dough during the evening or at night at least four times per week.
2. Eating carbohydrates in the evening or at night at least four times a week, between meals, with a carbohydrates to protein ratio greater or equal to 6:1.
3. The craving occurs along with the presence of dysphoria, which is alleviated by eating these foods.

This craving, therefore, would be an irresistible desire to consume sweets, food prepared with dough, or “junk” in response to a negative mood component, which would apparently be alleviated by this consumption. This would differentiate it from cravings for other nutrients, such as protein for example, where feelings of fatigue are typically experienced after consumption (32).

Neurobiology of Carbohydrate Craving

The underlying neurobiological mechanisms in the comorbidity continue to be controversial, and there are currently a number of hypotheses surrounding the phenomenon of carbohydrate craving in mood states (33).

The theory that has received the most attention is the serotonergic hypothesis, given that the neurotransmitter serotonin fulfills regulatory functions of the appetite, mood, and of the preference for certain nutrients. It has been proposed that when serotonin levels are low, appetite and carbohydrate craving are stimulated as a form of “self-medication,” due to the increase in cerebral serotonin after consumption (34). The decrease in serotonergic tone in mood disorders is well-known; the presence of carbohydrates increases the synthesis of serotonin (through an increase in tryptophan), in contrast to what occurs with other macronutrients such as proteins (35).

Counter to this theory, there is evidence that the serotonin increase process secondary to the increase in cerebral tryptophan would take at least 60 minutes to be completed (36). In turn, various studies show that the effect of carbohydrate consumption on negative feelings would be instantaneous, thus revealing a striking discrepancy among these data (37). Moreover, other studies have demonstrated that the increase in tryptophan due to carbohydrate consumption is too low to cause a significant increase in central serotonin levels; added to this is the finding that the increase in plasma tryptophan can be blocked with just 4% of proteins bound to carbohydrate-based food (38).

Due to the aforementioned, the serotonergic theory is an interesting hypothesis but insufficient for a complete understanding of the relationship between mood and carbohydrate craving. Other theories on this topic have emerged, primarily about the relationship between palatability mechanisms (understood as the quality of having a specific food be pleasing to the palate) and the hedonic response, which could be exacerbated under conditions of stress (36).

The evolutionary aspect is worthy of consideration to gain a possible understanding of carbohydrate craving. Identifying the most efficient nutrients is an adaptive capacity of human beings. Carbohydrate craving could be a biological part of the evolutionary behavioral system of the species (39). This is consistent with the intensification of the craving in stressful situations as part of a phylogenetic selection process, probably because it increases the possibility to rapidly store energy available in the environment to be able to confront aversive stimuli (40). Therefore, it has been suggested that the carbohydrate craving mechanism as an emotional regulator would have been evolutionarily selected due to its environmentally-adaptive role (39, 40).

Mood and Carbohydrate Craving

In terms of craving that refers specifically to food or specific food, it is known that up to 97% of women and 68% of men report the presence of some type of food craving at some point in life (41). Out of all types of nutrients studied, carbohydrates have garnered the most attention, primarily due to the great prevalence of this behavior in patients with psychiatric pathology, classically, for example, in Premenstrual Syndrome and Seasonal Affective Disorder (SAD), and in overweight patients (42).

A significant portion of the literature on carbohydrate craving pertains to its relationship with dysphoric mood. Thus, it has been considered that dysphoria would motivate this craving due to a deficit in serotonin, which would promote the craving because the intake of carbohydrates increases the central synthesis of serotonin. It is believed that the increase in serotonin would decrease dysphoria, thereby explaining the connection and interdependence between dysphoria and consumption of carbohydrates (43).

The described phenomenon is evident in patients with SAD, who increase their craving for carbohydrates in depressive episodes, particularly in the winter. Overall consumption of carbohydrates in these patients also increases in depressive episodes and there are studies that show impro-

vement in dysphoric mood symptomatology after consumption. It is worth highlighting that this relationship between mood and carbohydrate craving has also been observed in the general population, in which the most common craving is for carbohydrates, particularly in young women where there tends to be an association with mood symptoms such as anxiety, fatigue, and depression; the greater the mood component, the greater the intensity of the craving. This is in contrast to craving for other types of macronutrients where negative mood states are not prevalent prior or subsequent to intake, but rather components such as hunger, boredom, satiety, happiness, and energization (44).

Carbohydrate Craving and Bipolar Disorder (BPD)

There is limited evidence of a specific relationship between BPD and carbohydrate craving. The most relevant empirical data refer to the presence of this craving in patients with Seasonal Affective Disorder (45), a disorder that has a significant conversion rate to BPD over the long term, and which has been considered by various authors as a variant within the bipolar spectrum (46). Nevertheless, current research has focused on the hypothetical relationship between bipolar disorder and spectrum, on the one hand, with various eating disorders on the other hand, particularly with binge eating disorder and mixed eating disorders (47). This has impeded a specific clinical evaluation of craving and it has caused theories on self-medication based on mood improvement after the consumption of carbohydrate-rich foods to lose importance. This is the result of the absence of specificity regarding the type of macronutrient entailed in the binge, due to the emphasis on the negative affects associated with bingeing, and the exclusion of patients with craving even without the presence of weekly binges (48) (Appendix 1). However, there is currently evidence that the association between BPD and the presence of broad criteria of binge disorders or eating disorders could constitute a clinical and gene-

tic sub-phenotype within BPD, beyond the high comorbidity between both disorders, which reaches rates of up to 30% among patients with a diagnosis of BPD Type I, BPD Type II, and Schizoaffective disorder bipolar type, even more in patients with a rapid or ultra-rapid cycling profile. The clinical symptomatology evaluation related to eating disorders, particularly in young subjects, female, with significant anxious components, suicidality, marked mood instability, or BMI alteration, is therefore relevant, given the greater burden of psychiatric and medical pathology in these patients.

CONCLUSIONS

In general terms, for clinicians dedicated to Mood Disorders, the presence of various Eating Disorders as prodromes, markers of onset of the disease, or as residual symptoms, is not surprising in the long-term evolution of these patients. Clinicians differentiate carbohydrate craving, which is many times characteristic in the symptomatologic profile of Mood Disorders, from other types of craving, such as craving related to stress, which does not have a circadian component and is not specific to any type of macronutrient. However, the presence of eating pattern disturbances in Mood Disorders has not received attention in the literature that is commensurate with its importance in clinical practice. It has been validated in this review that the literature on this topic is very deficient; however, this issue is of utmost importance in the cross-cutting clinical evaluation of patients, in the assessment of long-term evolution, and in consideration of associated or secondary medical comorbidity as a risk factor. Given the long-term commitment entailed in BPD, nutritional management of these patients is highly important, particularly in patients with a strong component of impulsivity and emotional deregulation, and in whom eating-habit interventions could have a significant long-term impact. Likewise, the implications of therapy schemes are evident, in terms of considering agents that target both cases, or at least that do not exacer-

bate the intensity of the other symptoms or symptomatic profile (18).

The field of possible comorbidity between Mood Disorders and Eating Behavior does not appear to have defined direction nor agreement surrounding basic research criteria. Therefore, there is not yet any clarity regarding how much the knowledge of physiopathology of both entities could be elucidated with the comorbidity study. What we do know is that the literature and research still have a long way to go to catch up to the clinicians who not only recognize the frequency of comorbidity, but also a certain specificity in this frequency. Our hope is for this gap to be bridged through research efforts that must absolutely be independent and academic, because the field we are describing is removed from commercial interests; but, it needs to be close to the interest in understanding the most intimate mechanisms of disorders that cause serious disturbances in vast populations of patients who deserve a deeper understanding of this issue due to the implications it could have in their evolution.

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APPENDIX 1:

DSM-5 Diagnostic Criteria for Binge-Eating Disorder 307.51 (F50.8) :

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:

1. Eating, in a discrete period of time (for example, within any 2-hour period), an amount of food that is definitely larger than what most people would eat in a similar period of time under similar circumstances.

2. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).

B. The binge-eating episodes are associated with 3 (or more) of the following:

1. Eating much more rapidly than normal.

2. Eating until feeling uncomfortably full.

3. Eating large amounts of food when not feeling physically hungry.

4. Eating alone because of feeling embarrassed by how much one is eating.

5. Feeling disgusted with oneself, depressed, or very guilty afterwards.

C. Marked distress regarding binge eating is present.

D. The binge eating occurs, on average, at least once a week for 3 months.

E. The binge eating is not associated with the recurrent use of inappropriate compensatory behavior as in bulimia nervosa and does not occur exclusively during the course of bulimia nervosa or anorexia nervosa.

Specify if:

In partial remission: After full criteria for binge-eating disorder were previously met, binge eating occurs at an average frequency of less than one episode per week for a sustained period of time.

In full remission: After full criteria for bin-

ge-eating disorder were previously met, none of the criteria have been met for a sustained period of time.

Specify current severity:

The minimum level of severity is based on the frequency of episodes of binge eating (see below). The level of severity may be increased to reflect other symptoms and the degree of functional disability.

Mild: 1-3 binge-eating episodes per week.

Moderate: 4-7 binge-eating episodes per week.

Severe: 8-13 binge-eating episodes per week.

Extreme: 14 or more binge-eating episodes per week.

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