Food and mood: relationship between food, serotonin and affective disorders


The relationship of food and eating with affective and other clinical disorders is complex and intriguing. Serotonergic dysfunction in seasonal affective disorder, atypical depression, premenstrual syndrome, anorexia and bulimia nervosa, and binge eating disorder is reviewed. Patients exhibiting a relationship between food and behaviour are found in various diagnostic categories. This points to a need to shift from nosological to functional thinking in psychiatry. It also means application of psychopharmacological treatments across diagnostic boundaries. The use of phototherapy and psychotropic drugs (MAO inhibitors and selective serotonin reuptake inhibitors like fluoxetine) in these disorders is discussed.

Der Mensch ist, was er isst (Man is what he eats) – Ludwig Feuerbach (1804–1872)

Through the act of food intake, the biological and cultural factors of the external world meet the biological and psychological factors of the individual's internal world. Eating is influenced by various factors far beyond the mere nutritional value of the food and the dietary needs of the individual. Such factors include economic conditions, culturally-imposed ideals of body shape, life events, stress, mood states, learned preferences and aversions, attributes, beliefs and cognitions, and other psychological conditions, sensory/hedonistic aspects of food, and brain chemistry (1). Eating is more than just food intake: eating plays an important role in our social interactions, and it can also be used to alter emotional states, and even to influence brain function.

Appetite and satiety

Appetite is essential for the maintenance of life. It is also a biopsychosocial phenomenon that arises as the end product of the intimate and complex interactions between the physiological processes of the individual and the environment (1). The appetite control system regulates energy and nutrient intake in order to maintain the homeostasis of the biological processes, and to ensure the adaptation of the individual to the environment. However, the regulation of the balance between nutritional requirements and nutritional supply is not symmetrical. In the case of undersupply of food, the regulatory mechanisms generate the drive to eat, or hunger. In contrast, in our affluent societies the abundant supply of palatable food with a high density of energy (high fat and/or carbohydrate content) tends to promote overconsumption and to result in weight gain, especially in individuals with genetic or other vulnerability to develop obesity. Therefore, the appetite control system shows a strong defence against undereating, but a rather weak defence against overeating.

Several neurotransmitters participate in the regulation of appetite, including serotonin (2), noradrenalin, cholecystokinin (CCK), endogenous opioid peptides, neuropeptide Y, and peptide YY. The paraventricular and ventromedial nuclei of the medial hypothalamus are involved in controlling energy balance, while the circadian pattern of eating is determined by the suprachiasmatic nucleus (3). Serotonergic stimulation of these nuclei results in satiety and leads to the termination of eating.

Dietary tryptophan and brain serotonin

Serotonin, or 5-hydroxytryptamine (5-HT), is a neurotransmitter that plays an important role in the regulation of circadian and seasonal rhythms, the control of food intake, sexual behaviour, pain, aggression, and the mediation of mood. Dysfunction
Food and mood: Relationship between food, serotonin and affective disorders

of the serotoninergic system has been found in a wide array of psychiatric disorders: depression, anxiety, disorders of the sleep-wake cycle, obsessive-compulsive disorder, panic disorder, phobias, personality disorders, alcoholism, anorexia nervosa, bulimia nervosa, obesity, seasonal affective disorder, premenstrual syndrome, and even schizophrenia.

With respect to the relationship between nutrition and behaviour, 5-HT is interesting in many ways. The synthesis of serotonin in the central nervous system depends on the dietary supply of the precursor amino acid tryptophan (TRP) (4). The first step in the synthesis of 5-HT is the uptake of TRP from the blood across the blood-brain barrier into the brain. In the neuron, TRP is converted to 5-hydroxytryptophan catalyzed by the enzyme tryptophan hydroxylase. Finally, 5-hydroxytryptophan is converted by the enzyme 5-hydroxytryptophan decarboxylase to serotonin. The rate-limiting step in the synthesis of 5-HT is the hydroxylation of tryptophan to 5-hydroxytryptophan. The enzyme tryptophan hydroxylase has a poor affinity for its substrate TRP, i.e., the enzyme is relatively unsaturated at the TRP concentrations normally found in the brain. Therefore, variations in brain TRP levels can change the substrate saturation of tryptophan hydroxylase, and as a consequence, rapidly alter the production rate of 5-HT (5).

The ingestion of TRP leads to rapid elevation in brain TRP and 5-HT levels. However, TRP and other large neutral amino acids (LNAAs: valine, tyrosine, leucine, isoleucine and phenylalanine) share a common competitive transport mechanism for crossing the blood-brain barrier. Thus, the transport of TRP to the brain does not depend on the absolute plasma level of TRP but on the plasma level of TRP in relation to the other large neutral amino acids. The plasma ratio of TRP to the other LNAAs is significantly influenced by macronutrient intake. A protein-rich meal contains relatively little TRP in contrast to the other amino acids, which compete with TRP for entry into the brain, and little TRP enters the brain. In contrast, high-carbohydrate (very low-protein) meals stimulate insulin secretion, which increases the uptake of LNAAs into muscle cells. As a result, the plasma ratio of TRP to LNAAs is greatly increased, and more TRP enters the brain with an increased 5-HT synthesis as a result (6).

The importance of the role of TRP as the precursor of 5-HT is demonstrated by the fact that TRP depletion has been shown to cause a rapid lowering of mood in normal males (7). TRP availability is also crucial to the action of antidepressants (8).

**Carbohydrate craving**

Increased serotoninergic activity results in the reduction of energy intake. 5-HT has also been postulated to play a role in macronutrient choice, with reduced serotoninergic activity leading to a preference for carbohydrates. According to the hypothesis of “carbohydrate craving”, some individuals have a strong need to consume carbohydrate-rich food (9, 10). This might be explained by the increased brain 5-HT synthesis following carbohydrate intake. These patients seem to prefer carbohydrates as a “self-medication” attempt, because they suffer from disorders in which deficient serotoninergic activity has been demonstrated, and because they typically report feeling better after ingestion of carbohydrates (11). However, the concept of carbohydrate craving has been criticized (12, 13). Despite its limitations, the hypothesis may be clinically helpful. The patient’s eating behaviour, especially dietary preference for carbohydrates, gives the clinician some clues about the underlying pathophysiology. This in turn may help in choosing the therapeutic approach.

**Eating disorders**

The prevalence of eating disorders has increased strikingly in recent years. Anorexia nervosa is characterised by severe weight loss caused by deliberate self-starvation, while bulimia nervosa is characterised by recurrent episodes of compulsive overeating, followed by attempts to avoid the consequences of positive energy balance by self-induced vomiting or other drastic means. The non-purging form of bulimia, also called the binge eating disorder (14, 15), is often associated with obesity. A certain type of obesity, the so-called carbohydrate-craving obesity, is associated with excessive carbohydrate intake, which might be caused by a defective feedback inhibition of carbohydrate intake after its ingestion (3, 9).

The background of eating disorders is complex, and probably involves dysregulation of several neurotransmitter systems. The involvement of impaired hypothalamic serotonin function in these disorders is well documented (3, 16). Such dysfunction could contribute to the onset, progression and persistence of symptoms. In particular, there is good evidence from experimental and clinical studies to suggest that serotoninergic dysfunction creates vulnerability to recurrent episodes of large binge meals in bulimic patients. Similarly, serotoninergic drugs like fluoxetine have been shown to be effective in controlling bulimic episodes and binge eating (17). Fluoxetine and other serotoninergic drugs, among them fenfluramine, are also used in the treatment of obesity (18, 19, 20).
There is also evidence that bulimic behaviour has a mood-regulating function, i.e., binging and purging are used by the patients to relieve psychic tension. However, bulimic behaviour seems to have different functions for different subgroups (21). Binging may be used to relieve anxiety, but it may result in an increase in guilt and depression (22).

**Seasonal affective disorder**

A typical patient with seasonal affective disorder (SAD) suffers from lack of energy, depressive mood, social withdrawal, hypersomnia, and hyperphagia with resulting weight gain, during the dark winter months (23). Often the patient is more disturbed by the lack of energy than by the low mood itself. Women are more likely than men to develop SAD. Craving for carbohydrates has been observed in two-thirds of the patients, whose major depression has a seasonal pattern, compared to one-fourth of patients without seasonal periodicity (24).

However, only some SAD patients have seasonal changes of body weight, which is related to a difference between summer and winter in starch-rich food intake (25).

These patients typically consume food with a high glycemic index like pasta, bread, potatoes, rice and corn during winter. They often report doing this to elevate mood and alleviate fatigue. While normal controls feel sedated following carbohydrate ingestion (26), SAD patients report activation (27). Carbohydrate craving of SAD patients is suppressed by summer, bright light treatment (25), tryptophan, fenfluramine, monoamine oxidase inhibitors (MAOIs), and selective serotonin reuptake inhibitors like fluoxetine (23).

Serotonin is involved in the pathophysiology of SAD. Hypothalamic 5-HT content falls in the winter even in normal individuals (3). The transmission of information about seasonal and circadian rhythms is thought to proceed from the retina to the circadian pacemaker in the suprachiasmatic nucleus, and then to the paraventricular nucleus in the medial hypothalamus (25). Photoperiod can thus influence various metabolic processes. Through retinal mechanisms, light therapy might lead to decreased release of noradrenaline and/or increased release of serotonin in the medial hypothalamus, which in turn would alleviate the atypical symptoms of hyperphagia and hypersomnia in SAD (25). The decrease of environmental light during winter may cause a greater drop of 5-HT in individuals susceptible to developing SAD. The role of CNS 5-HT deficiency in SAD is also supported by good treatment results with serotonin agonists. However, bright light treatment is considered to be the method of choice (23).

The SAD patients also show a high rate of major affective disorder, including SAD, and alcohol abuse in their families, suggesting a genetic or familial origin of the disorders of the serotoninergic system. According to our clinical experience, many SAD patients also exhibit comorbidity with other disorders linked to serotoninergic dysfunction, like premenstrual syndrome, alcohol abuse, and overweight.

**Premenstrual syndrome**

Premenstrual syndrome (PMS) refers to emotional, behavioural and somatic symptoms experienced during the late luteal phase of the menstrual cycle. Many women have premenstrual symptoms, but only 2 to 10% of menstruating women are estimated to suffer from symptoms severe enough to interfere with normal functioning (28). In the Diagnostic and Statistical Manual of Mental Disorders, Third, Revised Edition (DSM-III-R) of the American Psychiatric Association the syndrome is called late luteal phase dysphoric disorder. The typical symptoms are depressive mood, mood swings, irritability, fatigue, concentration difficulties, hypersomnia, anxiety, and increased appetite.

Many women with PMS report carbohydrate craving during the premenstrual week (29), but some of them also show a preference for carbohydrates throughout the menstrual cycle. There is a high rate of comorbidity with other psychiatric diagnoses, especially affective disorders (30).

The etiology of PMS is unknown, but theories and treatments abound. These theories include dysfunction of the serotoninergic system, circadian rhythm abnormalities, altered levels of estrogen and progesterone, and disorder of the renin-angiotensin-aldosterone system.

PMS and major depression may be related. This is suggested by the high rate of a history of depression, and an increased risk of developing depression later in PMS patients. These two disorders may therefore have some abnormalities in common. According to the phase-advance hypothesis of affective disorders, the central neural oscillator in the hypothalamus regulating the circadian rhythms of the body is phase-advanced (shifted earlier) in relation to the sleep-wake cycle (31). A similar phase-advance of circadian rhythms has also been observed in PMS, and consequently, bright light treatment in the evening (32) and sleep deprivation (especially late-night partial sleep deprivation) (31) have been effective.

In view of the critical role of serotonin in the regulation of circadian rhythms and in the regulation of appetite, carbohydrate craving in PMS can be seen as an attempt at self-medication. In accordance with this hypothesis, the selective serotonin re-
uptake inhibitor fluoxetine effectively suppresses carbohydrate craving and other PMS symptoms (28).

**Atypical depression**

Some depressive patients do not have classical symptoms of depression (e.g. loss of appetite, decreased sleep, psychomotor agitation), but instead show hyperphagia, hypersomnia, extreme fatigue, chronic sensitivity to rejection, and mood reactivity (33, 34). The lifetime prevalence of this atypical depression is estimated to be 0.7 % (35). Compared to subjects with major depression without atypical features, subjects with this disorder have a younger age of onset, more psychomotor retardation, more comorbidity with panic disorder, drug abuse or dependence, and somatization disorder (35). Atypical depression might therefore be a distinct subtype of major depression that is responsive to treatment with MAOIs (33, 34). Antidepressants may also be useful in mildly depressed patients with atypical features (36).

Reversed neurovegetative signs of hypersomnia and weight gain, in combination with motor retardation, fatigue and volitional inhibition, are often seen in bipolar depression. This form of depression is also called anergic depression (37, 38). MAOIs, either alone or combined with lithium, are effective in treating this condition (37, 38).

Another subtype of atypical depression is hysteroid dysphoria (33, 34, 39), which is characterized by histrionic and narcissistic features. Individuals with this disorder, who are usually but not exclusively women, show a romantic preoccupation, seeking romantic attachment, approval and praise. They exhibit rejection sensitivity and often develop episodes of atypical depression after the loss of a romantic attachment. "Self-medication" with sweets or chocolate is reported in hysteroid dysphoria (39). It is not clear, however whether the patients crave carbohydrates for their gratifying aspects (sweetness, high fat content, palatability), or whether this is an attempt to regulate brain serotonin and thereby to elevate mood (39).

**Clinical implications**

There is one subgroup of patients who exhibit characteristic symptoms compatible with the hypothesis of the relationship between food, mood and behaviour. In these "food and mood" disorders, serotonin deficiency in the CNS seems to play a major role, and eating behaviour can be seen as a self-healing attempt. However, this self-medication is often not effective enough and may even lead to a vicious circle, and pharmacological interventions are called for.

The effects of food on mood and vice versa in ordinary clinical populations often go unrecognized. These patients often report that their disorder has rarely been recognized by their doctor. The patients can describe how, in contrast to their "ordinary" psychological problems, their particular symptoms of winter depression, lack of energy and carbohydrate craving are "beyond their control". They may even spontaneously recognize the self-medication aspect of their eating behaviour.

It is therefore important for the clinician to be aware of these connections. When compiling the patient's history, the clinician should ask the crucial questions about the patient's mood, eating behaviour, possible dietary preferences, weight changes, seasonal patterns, family history of affective disorders, eating disorders, obesity, and alcoholism, and the effects of food on mood.

Because of the overlap between and coexistence of the various syndromes (comorbidity), the prevalence rates of these "food and mood" disorders in the general population are difficult to estimate. For seasonal affective disorder, anorexia and bulimia nervosa, binge-eating disorder, premenstrual syndrome and atypical depression, we can put forward a very rough estimate that at least 2 to 5 per cent of the population are suffering from these disorders. Most patients with a clear connection between eating and their affective states also have signs of the disorders discussed in this paper. A female patient with a family history of depression and alcoholism might, for instance, describe symptoms of carbohydrate craving (preference for pasta, bread, pastry, bananas, chocolate), overweight, PMS and winter depression.

Knowledge of the symptom profile of the patient allows the clinician to plan a tailored treatment that might consist of psychoeducation, cognitive-behavioural therapy or other forms of psychotherapy, dietary therapy, bright light treatment, or pharmacotherapy with selective serotonin reuptake inhibitors or MAO inhibitors. Patients exhibiting a relationship between food and behaviour are found in several diagnostic categories. This fact underscores the need for a shift from traditional nosological to modern functional thinking in psychiatry, and consequently, the application of psychopharmacological treatments across present diagnostic boundaries (40).

The relationships between food, eating and mood are complex and intriguing, and further study is clearly needed.

**References**

Wallin and Rissanen
