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# Current Concepts in Food Addiction

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We all experience cravings once in a while and we all overeat on occasion. We are generally aware of what we are doing, sometimes regret it afterwards, but generally recognize it as atypical behaviour, something that is not likely to be repeated too often. What would happen, however, if this behaviour became more frequent, if cravings became harder to ignore and overeating became the norm rather than the exception? What would happen if eating became the focus of most activity to the detriment of social functioning and began to cause harm to your health? And what if withdrawal from food caused anxiety, irritability and altered mood? When does craving become addiction?

The past decade has seen the diagnosis of "food addiction" (FA) propelled from lay literature conjecture to the front page of esteemed scientific publications, a move fuelled by research into the alarming rise in obesity. It fell just short of recognition in the DSM-V released earlier this year, but not without substantial lobbying and controversy.

While it is apparent that not all overweight or obese individuals suffer from food addiction, and similarly, not all those with food addiction are obese, an understanding of the mechanisms controlling appetite, craving and addiction is essential for those treating weight-related health issues.

The aim of this article is to give an overview of the current theories behind appetite control, food cravings and food addiction. By detailing the neurophysiology of these conditions, groundwork is laid for an approach to diagnosis and treatment.

## Appetite, satiety and craving

The innumerable interactions within the brain and between the brain and the body systems associated with nutrition and metabolism continue to unfold, creating an ever more complex web of feedback loops and neuroendocrine control mechanisms. However, it would appear that there are two separate but interlinked systems that contribute to the control of food intake. The first is a ***homeostatic*** system that integrates metabolic needs with food-related satiety messages. The second is a ***reward*** pathway that mediates the hedonistic value of food along with motivational behaviour and neocortical rationality.

The ***homeostatic system*** within the hypothalamus (arcuate nucleus, lateral hypothalamus and paraventricular nuclei) incorporates hunger and satiety centres that direct us toward feeding or resting behaviour. The predominant primitive drive is to eat, a message mediated by neuropeptide-Y (NPY) and agouti-related peptide (AGRP) from the arcuate nucleus (ARC). This message is turned off by a number of satiety messengers that provide peripheral feedback from ingested food and metabolic state plus neural control within the brain. The most important peripheral endocrine messengers are insulin and leptin, which provide satiety signals based on both the consumption of food and the status of the body's energy supplies, most notably, fat stores. Other messengers include glucose, ghrelin (promoting hunger), PYY, CCK and GLP, which all act on the hypothalamus to control the balance between hunger and satiety.[1,2]

The ***reward system*** is more complex and incorporates a larger number of brain areas and pathways. Humans (and other higher functioning animals) can eat or starve independently of basic hunger-satiety messaging.[3] We act on situational, emotional and hedonistic cues, allowing such activity as ordering chocolate dessert despite feeling full from previous courses. The ventral tegmental area is the initial site of activation through opioid, nicotinic and cannabinoid receptors, releasing dopamine through the mesolimbic dopamine system (MDS) to the nucleus accumbens (NA) and limbic system. This is the initial key pathway involved in reward (and addiction), its primary role being the promotion of motivational behaviour in response to reward-predicting stimuli. While essential in mediating the acutely rewarding value of drugs or food, it has a secondary, longer-term effect to promote need or craving. These so-called "wanting incentives" or "incentive salience" are inherent to most animals.[4-7]

The nucleus accumbens (NA) receives input from the MDS, limbic system, amygdala (AMY), pre-frontal cortex (PFC) and hippocampus, allowing it a central role in the mediation of reward-based behaviour. In humans, the ability of certain drugs (such as cocaine, alcohol and nicotine) to release dopamine (DA) in the nucleus accumbens leads to "artificial reward" and hence addiction.

Similar neurochemical stimulation is seen with highly processed sugary or fatty foods and provides the basis for some aspects of food addiction.

The amygdala (AMY) is a primary processing area and receives information about the perceived metabolic "value" of food as well as its hedonistic or pleasurable value such as taste.[4] It mediates the addictive properties of cocaine via dopamine D-1 receptors, and alcohol via GABA and opiate receptors.

Thus, while the MDS appears central to addiction, other dopamine-independent pathways act via numerous circuits to provide reinforcement and reward-seeking behaviour.

Craving was originally thought to be simply one end of the homeostatic spectrum, an extreme version of hunger resulting from food deprivation. This "restrictive theory" has empirical support[5] yet fails to explain craving triggers in humans such as emotion, boredom and stress. It is this strong emotional element of craving that makes it a far more complex aspect of hunger and satiety than the neuro-hormonal feedback implicated by simple physiologic homeostasis.[8] It is now believed that the mesolimbic dopamine system, which is intricately involved in addiction, is the one of the key subconscious triggers for craving and its attendant behavioural sequelae. Serotonin also exerts a strong influence on craving although this relates primarily to the emotional control of eating rather than the reward system. Certain foods, including chocolate and other sweets, increase serotonin in the brain and become desirable in low-serotonin states such as depressed mood, pre-period and during the initial stages of dieting.

## Dopamine and addiction

The past ten years have seen a tremendous amount of research into the role DA plays in addiction. While certain drugs (such as cocaine) have the ability to acutely and dramatically raise dopamine activity in the limbic system with resultant euphoric psychomotor effects, this effect is not noted with all addictive substances (such as alcohol). It now appears that the MDS has a central and profound influence over the way we react and respond to stimuli that we consider ***potentially rewarding***. Under the influence of numerous factors, including the intake of "addictive" or rewarding substances, or indeed rewarding activity (gambling for example), the MDS undergoes neurochemical remodelling. This reorganization of reward and memory circuits leads to a heightening of what is termed "incentive salience".[9] This is the emotional "wanting" attribute given by the brain to stimuli that predict reward. So, for someone addicted to alcohol, the mere visual stimulus of a bottle or glass will increase DA activity, create craving and drive behaviour toward consumption. Similarly, it would be the sight or smell of food, or even a restaurant sign, that would lead to craving and eating. It is this incentive salience that makes withdrawal so difficult as neurochemical pathways are activated by remote stimuli even when trying to avoid the substance itself.[10] The altered MDS makes these cravings impossible to ignore as they are promoted in importance above all other activity. To further exacerbate this response, prolonged MDS dopaminergic activity impairs the normal rational and cognitive control over impulsive behaviour exerted by the PFC. This dissociation of cortical and subcortical systems with resultant impairment of decision-making and avoidance of impulse is a feature that addiction shares with chronic stress, as we shall see later.

The "reward deficiency" theory[11] suggests that in obesity, altered Type-2 dopamine receptor (DA-D2) availability or sensitivity leads to increased demand for dopaminergic stimulation and thus increased intake of rewarding substances. Relative DA deficiency would therefore induce eating behaviour that promises to raise dopaminergic signalling. This would also explain the tendency of individuals to eat palatable food on withdrawal of nicotine (a dopaminergic stimulator) or while taking antipsychotic medication that reduces DA levels.[12] Although intuitive, the picture is likely more complex. One interesting paradox is the fact that DA is known to have two separate effects on the nucleus accumbens (NA) and hypothalamus[13] While increased DA activity in the MDS promotes food-seeking behaviour, it simultaneously exerts a controlling affect on hunger and food consumption by inhibiting NPY, an effect augmented by satiety messengers such as leptin. In addition, the NA receives other dopaminergic inputs from the *dorsal striatum*, a mechanism thought to be involved with survival and the maintenance of adequate calorie intake. Drugs that block DA-D2 receptors cause increased appetite and weight gain while agonists cause anorexia. Although there is argument as to whether this DA-D2 abnormality is primary or secondary, there is certainly a clear association and in some cases a genetic predisposition. A plausible argument is that the MDS exerts its motivational effect on the NA via Type-1 dopamine receptors (DA-D1), while DA-D2 receptors mediate feedback regulation of hunger, eating behaviour and compulsion in order to limit over-consumption.[14,15] Thus, food addiction in obesity would also be considered a failure of adequate feedback in common with other aspects of the condition including leptin and insulin resistance.

## Factors promoting food addiction

**Stress –** Acute and chronic stress have a profound effect on the neurophysiology of subcortical structures. At its simplest, the hypothalamus-pituitary-adrenal (HPA) axis provides a primitive protective response to threatening stimuli, the classic sabre-toothed tiger. However, our modern lifestyles provide an excess of predominantly "perceived" and non-resolving threats, which over-stimulate this system and result in harmful neural and endocrine dysfunction. Adrenal fatigue is well recognized and leads to an impaired response to true physical stressors such as inflammation or infection. Less known but more profound is the development of cortisol resistance leading to disruption of feedback within the HPA system. Subsequent increased corticotropin releasing hormone (CRH) production in the hypothalamus and associated changes within subcortical structures including the amygdala have significant effects on a number of systems including the hunger-satiety centre and the reward pathway. Acute stress and cortisol increase DA release in the NA,[16,17] which as we have seen, leads to reward-driven behaviour. Stress and anxiety further sensitize the MDS and

amygdala to promote this behaviour while simultaneously causing atrophy in the hippocampus and PFC resulting in even less control over impulsive behaviour and craving.[16]

Thus, acute stress will promote craving, seeking and eating of highly palatable sweet or fatty foods in order to satisfy and reset the pathway. Chronic stress will enhance this pathway and reduce cognitive control leading to ever-escalating desire and ingestion of calorific foods, weight gain and metabolic syndrome.

Further interesting research has found that chronic stress reduces DA activity[18] and alters the DA-D2 receptor making it less sensitive to DA. This receptor co-exists with the ghrelin receptor (GHSR-1), which, as we know, is responsible for intense feelings of hunger. As the DA-D2 receptor modulates the effect of ghrelin, any decreased efficacy will only heighten craving in food addiction, obesity and stress.

**Food content –** Processed, highly calorific foods rich in fats and sugars affect both the homeostatic mechanisms that normally control food intake and the hedonistic reward pathways that influence whether we eat for pleasure. As a result of an effect called "epigenetics", environmental factors can profoundly influence gene expression and thus physiologic function.[19] Diets high in saturated fats increase the production of and sensitivity to NPY, AGRP and the orexins, our neural hunger messengers while inhibiting the satiety messenger alpha-MSH. In addition they reduce sensitivity to peripheral messengers such as insulin, leptin and CCK. Palatable foods stimulate the reward system through a number of pathways by increasing levels of endogenous opioids and stimulation of "pleasure" receptors such as GABA and benzodiazepine. Increased activity in cannabinoid receptors also occurs and promotes hunger. Through these various mechanisms palatable foods increase dopamine production and adjust the neural "set-point" such that any reduction in DA levels leads to anxiety and craving. The role of our food environment cannot be understated. The heavy marketing of "fast" and processed foods, the inclusion of high-fructose corn syrup and the relative cheapness of poor quality "addictive" foods is considered by some as dangerous as having cocaine samples available at your local supermarket.

**Emotion and Serotonin** – Adequate serotonin promotes a sense of calm, security, relaxation and confidence, while low levels are associated with depressed mood, anxiety and irritability. Serotonin is widely considered to be the "anti-dopamine", diminishing reward-seeking behaviour and craving thus explaining why reduced levels in PMS, depression and dieting lead to a desire for sweet or starchy foods that temporarily increase serotonin levels.[20,21] This in itself can lead to overeating and weight gain. The interaction with obesity and food addiction is obviously multifaceted but it is clear that factors resulting in impaired serotonin production or sensitivity will serve to promote activity in the dopaminergic reward pathway and exacerbate craving along with food-directed behaviour.

**Genetics** – There appears to be some evidence of a genetic susceptibility to obesity and food addiction that may predispose an individual to these conditions, but in the absence of other emotional and environmental factors is not sufficient in most cases to be a cause. These include reduced DA-D2 receptor numbers and sensitivity along with enhanced activation of brain areas involved with processing food palatability.[19,22]

## Diagnosis of Food Addiction

Understanding the neurophysiologic basis of food addiction helps direct us towards an accurate diagnosis, something of utmost importance when planning treatment. However, we need to distinguish food addiction from other conditions, particularly eating disorders such as binge eating and bulimia and simple overeating.[23-25,27]

The American Society of Addiction Medicine (ASAM) gives the following short definition of addiction:

"Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death."

Our understanding of food addiction certainly fits this picture yet there is on-going discussion as to whether physiologic and diagnostic criteria for addiction to recognized substances of abuse can be applied to food. Although perhaps less acutely toxic than, for example, cocaine, the neurochemical pathways involved and dysfunctional outcomes resulting from the ingestion of sweet, fatty and processed foods are identical (Table 1).

**TABLE 1**
**Neurochemical changes during the 3 stages of addiction**

| | |
|---|---|
| 1. **Binge/Intoxication** | • MDS/Opioid pathway stimulation<br>• Stimulus-response pathways engaged |
| 2. **Withdrawal/ Negative Affect** | • Decreased MDA stimulation, decreased serotonin.<br>• Decreased mood, activity and motivation for other tasks<br>• Increased activity of HPA axis – anxiety |
| 3. **Preoccupation/ Anticipation (Craving)** | • Reorganization of reward/memory circuits<br>• Impaired PFC + Amygdala dysfunction – loss of control<br>• HPA/CRF sensitivity |

Binge eating disorder is classified in the DSM-V and includes a number of diagnostic criteria that show significant overlap with the features of food addiction.

Gearhardt et al[23] argue convincingly that food addiction fits into the parameters of the DSM-IV Substance Dependence category, arguing that the legality and availability of food makes some of the social aspects of the condition less obvious than might be found with drugs. For the practising clinician, however, there are some important differences, which may allow us to differentiate between binge eating disorder (BED) and food addiction. Firstly, in BED, there is little craving or compulsion to eat on a regular basis and individuals frequently have negative feelings toward food. This contrasts to the craving and overeating associated with FA and the need for high fat or sugary foods to feel normal. BED is considered an "expressive disorder" associated with underlying emotional or psychological dysfunction, something not found in FA. In FA, triggers to eat are primarily food based rather than emotional, although, as we have seen, emotional input can influence the development or progression of food addiction. Withdrawal occurs in some, but not all subjects with FA, leading to heightened HPA activity when unable to satisfy their food triggers. This is not seen in BED. Finally, although counterintuitive, the incentive salience associated with FA results in far less control of food intake than BED. Another useful and validated diagnostic tool, which incorporates a number of physical and emotional factors along with a food diary, is the ***Yale Food Addiction Scale.***[26]

## Treatment for food addiction

The National Institute on Drug Abuse (NIDA) advises a four-step program for addiction; detoxification, medication, behavioural therapy and relapse prevention. The aim is obviously to remove intake and dependence on a substance entirely. While the steps involved in the treatment of food addiction may be similar, the goal is the avoidance of *certain* foods rather than *all* foods. In addition, the prevention of relapse may be more difficult due to the omnipresence of triggering stimuli, a factor easier to control in drug or alcohol therapy.

My approach changes the order of the above steps. Initial detoxification, which, in drug/alcohol abuse is often completed under controlled and monitored conditions, is impractical and likely to cause undue stress making success less likely. I focus on resetting hormonal and neurochemical imbalance first, which allows a less traumatic transition to detoxification.

### Step 1 – Rebalancing

Akin to stage 2, "medication", the rebalancing of hormonal and neurochemical systems is multi-modal, including changes to diet, behavioural modification and supplements. There are four primary aims; restoring satiety feedback, controlling HPA overactivity, modifying dopamine reactivity and increasing serotonin.

Satiety feedback incorporates a number of messengers but the predominant dysfunction involves leptin and insulin resistance. Depending on the individual and degree of addiction I may not enforce a strict diet with withdrawal of all addictive foods initially. However, I will recommend incorporating adequate protein at each meal and encouraging only three meals per day without snacking in order to reset insulin and leptin satiety signalling. I use L-Carnosine as a supplement to improve leptin sensitivity.

Due to its adverse effects on metabolism, satiety feedback and reward system dysfunction, correction of HPA axis overactivity is a key factor in the management of obesity and food addiction. I have found Serenitin-Plus, a casein decapeptide from milk known as *lactium*, to reliably reduce CRH/cortisol levels and re-establish feedback within the HPA system. I also address sleep disturbance and recommend lifestyle therapies such as meditation, massage therapy, exercise and music or laughter therapy.

Increasing dopamine levels through diet or supplementation is popular in the management of food addiction but is simplistic and ignores much of the newer research into functioning of the reward pathway. As such this approach may backfire and actually increase craving and food-seeking behaviour. My approach is to concentrate on promoting satiety feedback, rebalancing the HPA axis and increasing serotonin while cautiously increasing dopamine. In addition I would add omega-3 DHA supplementation to *increase* D2 receptor activity and *reduce* D1 activity.[28] The omegas will also help to increase serotonin and control cortisol.

As noted previously, the relative inactivity of the DA-D2 receptor in the D2-GHSR1 complex enhances the hunger-inducing effects of Ghrelin.[29,30] Therefore, minimizing ghrelin production is key. I use protein, fibre and fluids in the diet along with omega-3 supplements, which have been shown to promote D2 function.

Serotonin levels can be increased through a diet rich in tryptophan and with supplementation with 5-HTP. Sun exposure, exercise and laughter are behavioural therapies that can also increase levels.

### Step 2 – Detoxification

Detoxification involves primarily the withdrawal of trigger foods and restoration of a more normal healthy diet. In individuals with significant addiction I will delay this stage until rebalancing is complete, while in others I may commence it simultaneously. Detoxification involves both phase 1 and phase 2 naturopathic processes to help the body eliminate the inflammatory products associated with processed foods and environmental toxins. It will also help clear the excess hormones and neurochemical messengers, which have altered brain pathways and contributed to both food addiction and ill health.

### Step 3 – Behavioural Therapy

Although food addiction appears to have a relatively well-defined neurochemical basis, there are numerous personal, emotional and environmental factors that make the condition highly individual. As such, the behavioural aspect of treatment can be quite difficult and the involvement of other health professionals is recommended.

Firstly it is important to create a support system. Enlist people you admire and trust to provide encouragement and support your healthy lifestyle. Exercise is a key component of treatment, providing reward, reducing stress and improving metabolism and satiety. Bodywork including yoga, massage therapy, meditation and music or laughter therapy increases serotonin while reducing cortisol.

Cognitive behavioural therapy (CBT) is a type of psychotherapy that addresses dysfunctional emotions, maladaptive behaviours and cognitive processes through goal-oriented, systematic procedures. Under the care of a qualified practitioner this treatment modality can be central to the management of the psychological and emotional aspects of FA.

## Step 4 – Relapse Prevention

Perhaps one of the most difficult aspects in the management of any addictive disorder is the prevention of relapse or the development of "addiction transfer", the shifting from one addiction to another to maintain reward. Success in steps one through three minimizes this likelihood but given the perpetual exposure to triggers in daily life, the risk is substantial.

Removing all triggers within controlled environments such as home and workplace is key. Avoiding situations where triggers might exist is more difficult and needs to be balanced with the value of friendship, social interaction and healthy activity such as exercise. Having a supportive social group is essential and the "buddy system" can be extremely valuable when faced with a trigger crisis. Using techniques learned in CBT or meditation will also provide a defence against relapse.

**Food Addiction** is rapidly being recognized as playing a major role in the seemingly unrelenting rise in obesity seen in our population. Driven by a combination of factors including, most importantly, chronic stress and the availablity of processed high fat and sugar foods, this compex disorder may represent one of the most significant health issues of the twenty-first century. Understanding its causes and pathology is essential for naturopathic doctors given their pivotal role in the prevention and treatment of nutrition-related disease. By formulating a cohesive approach to diagnosis and treatment they are uniquely positioned to enable a significant and vital impact on the proliferation of food addiction in the coming years.

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## APPENDIX 1:
## Impact of Food Addiction on Health

**Metabolic:** obesity, type-2 diabetes, hypercholesterolaemia, hypertension, heart disease.

**GI:** cholecystitis/cholelithiasis, gastritis, constipation

**Emotional:** depression, anxiety, sleep disturbance, social dysfunction, poor self-esteem

**Nutritive:** vitamin/mineral deficiency.