



## Review

## The plausibility of sugar addiction and its role in obesity and eating disorders

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## SUMMARY

**Background & aims:** To consider the hypothesis that addiction to food, or more specifically sucrose, plays a role in obesity and eating disorders.

**Methods:** By considering the relevant literature a series of predictions were examined, derived from the hypothesis that addiction to sucrose consumption can develop. Fasting should increase food cravings, predominantly for sweet items; cravings should occur after an overnight fast; the obese should find sweetness particularly attractive; a high-sugar consumption should predispose to obesity. More specifically predictions based on the hypothesis that addiction to sugar is central to bingeing disorders were developed. Dieting should predate the development of bingeing; dietary style rather than psychological, social and economic factors should be predispose to eating disorders; sweet items should be preferentially consumed while bingeing; opioid antagonists should cause withdrawal symptoms; bingeing should develop at a younger age when there is a greater preference for sweetness.

**Results:** The above predications have in common that on no occasion was the behaviour predicted by an animal model of sucrose addiction supported by human studies.

**Conclusion:** There is no support from the human literature for the hypothesis that sucrose may be physically addictive or that addiction to sugar plays a role in eating disorders.

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## 1. Introduction

## Summary

- Following sugar consumption a rat model has demonstrated physiological and behavioural changes consistent with addiction, although it was consumed under a highly prescribed and atypical feeding procedure.
- By analogy with the rat data it has been suggested that human obesity and binge eating might reflect an ‘addiction’ to sucrose consumption, a suggestion that relies to a great extent on the suggestion that physical dependence occurs in a similar manner to that observed with drugs of abuse.
- The day to day food preference of rats reflects palatability rather than sucrose content.

## 1.1. General background

There is a widespread assumption that sugar consumption can lead to addiction: putting the words addiction and sugar together into the Google search engine produced 769,000 hits. A sample comment that illustrates the type of view often expressed in popular literature is that “sugar addiction can be just as strong as

a drug or alcohol dependency”. Although at one time such opinions were largely dismissed by the scientific community, more recently animal studies of bingeing on sugar<sup>1,2</sup> or fat<sup>3,4</sup> have reported findings that have been used to bolster the view that food can be addictive, although the conclusions drawn by the scientists themselves and those relying on their results can differ. Those who have carried out the research have tended to concentrate their attention on eating disorders,<sup>1,2</sup> whereas more popular writing can portray the phenomenon as widespread if not virtually universal.

If addiction to food can be established in humans there are widespread implications. Dieting might not be the optimal response to obesity as it will lead to counter-regulatory mechanisms such as cravings and withdrawal symptoms. In fact Trotzky<sup>5</sup> has treated eating disorders as addictive diseases using the twelve step programme that is familiar when considering addiction to other substances. If an animal model that is a homology of the human condition can be demonstrated, it would provide the means of establishing the underlying basic biology with consequent opportunities to establish novel treatments. There are also potentially widespread implications for food manufacturers and the fast-food industry. At an annual symposium of the “Confectioners Association and Chocolate Manufacturers Association” Susan Smith the Senior vice-president commented that: “They are looking at the tobacco model, turning their sights on sugar the same way they did on tobacco”. In 2003 Professor Banzhaf of George Washington

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University wrote to Burger King pointing out the possibility of future legal action: stating that "... foods of the type served at your fast food restaurants may produce addictive like effects ... research strongly suggests that ... at least some fast foods can act on the brain the same way as nicotine and heroin".

It is apparent that we need to establish the veracity of such claims. Given the importance that may be placed on the research that considers the development of food addiction in animals, the relevance of these findings to the human condition is presently considered. Although animal studies can generate hypotheses, they need to be confirmed in humans who in addition are influenced by a cultural and social environment that adds a complexity not seen with rodents. The plausibility that sugar addiction plays a role in food intake, obesity and eating disorders is therefore considered. The aim was to derive predictions from animal studies and then to establish the extent to which they are supported by human research. It is not the purpose to consider the animal research in detail although it is outlined initially to allow relevant predictions to be made.

### 1.2. Addiction – it depends what you mean

Definitions are arbitrary and the answer as to whether sugar is addictive may depend on how it is defined. For some, addiction is a pharmacological term characterized by a compulsion to consume that is driven by cravings. Tolerance occurs so that over time to achieve the same response you need to increase the dose. There is dependence so that there are withdrawal effects if consumption does not occur, making it difficult to quit. However, the term addiction has evolved leading some to designate this type of pharmacological definition as physical dependence.

Psychiatrists use the term dependence rather than addiction. The American Psychiatric Association criteria for the clinical diagnosis of abuse and dependence is a maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:

1. Recurrent substance use resulting in a failure to fulfil major role obligations at work, school, home
2. Recurrent substance use in situations in which it is physically hazardous
3. Recurrent substance-related legal problems
4. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance. (*Diagnostic and Statistical Manual-IV (DSM-IV)*)

At the other extreme a lay definition of addiction has developed that may amount to little more than giving a particular activity a very high priority. Never missing an episode of a favourite soap-opera might be so described. An element of compulsion is a further step with behaviour being clinically considered if the compulsion is uncontrolled, albeit there is no harm being suffered by the patient or others. Medically there is a distinction between physical dependence with characteristic withdrawal symptoms and psychological dependence that is "uncontrolled, compulsive use", even if nobody is harmed. Although an easy solution would be to reserve the term addiction for use with drugs of abuse, some feel that psychological dependency on such things as work, gambling, sex, computers, exercise, shopping, pornography or religion should be included. For others palatable food in general and sugar in particular should be part of this list. In practice these types of addiction are not always easy to distinguish as both physical and psychological mechanisms can co-exist.

Although there are many ways in which addiction has been defined a way of proceeding is required. Pelchat<sup>6</sup> noted that the majority of evidence relating to food addiction relies on the similarities and differences between food and drug cravings. The renewed interest in the possibility of sugar addiction relies to a great extent on the work of Hoebel<sup>1,2</sup> whose argument relies on drawing biological parallels between the response of the body to sugar and drugs of abuse. Therefore the present review will draw on physical dependency rather than the psychological definition of addiction or the use of clinical diagnostic criteria. This approach seems reasonable as they commented that "... 'Food addiction' seems plausible because brain pathways that evolved to respond to natural rewards are also activated by addictive drugs".<sup>1</sup> In this spirit 'sucrose addiction' is predicted to be associated with craving, tolerance and withdrawal symptoms. The present objective is limited to considering the view that sucrose consumption might result from physical addiction in a manner homologous to drugs of abuse.

### 1.3. A rat model

Avena et al.<sup>1</sup> reviewed the evidence that, given an appropriate feeding pattern, it is possible to show sugar addiction in rats. The starting point for this line of research was that: "Many people claim that they feel compelled to eat sweet foods, similar in some ways to how an alcoholic might feel compelled to drink. Therefore, we developed an animal model to investigate why some people have difficulty moderating their intake of palatable foods".

Rats were deprived of food for twelve hours and then given twelve hours access to food, starting four hours into the dark phase, when they could consume laboratory chow and depending on the study either a ten percent solution of sucrose or a twenty-five percent solution of glucose. After being kept on this schedule for a month the animals showed signs of addiction. During the first hour of access there was a large intake of sugar, a phenomenon described as a 'binge'; withdrawal symptoms were displayed; in a similar manner to drugs of abuse dopamine was released in the nucleus accumbens; opioid antagonists produced withdrawal symptoms.<sup>1</sup> Thus there was a body of research that supported the suggestion that rats kept under this behavioural regime manifest physiological and behavioural changes consistent with an addiction to sugar.

It was proposed that this animal model potentially offered insight into various human disorders. "We suggest that sugar, as common as it is, nonetheless meets many of the criteria for a substance of abuse ... The rise in obesity, coupled with the emergence of scientific findings of parallels between drugs of abuse and palatable foods has given credibility to this idea." The feeding regimen of the rats "shares some aspects of the behavioural pattern in people diagnosed with binge-eating disorder or bulimia. Bulimics often restrict intake early in the day and then binge later in the evening, usually on palatable foods".<sup>1</sup>

### 1.4. Sugar, sweetness or palatability?

The concept of 'sugar addiction'<sup>1</sup> relies on rats given the choice between a palatable sucrose solution and a much less palatable chow. Naturally in such circumstances they consume sucrose. The question is whether it is sucrose, sweetness or palatability to which they are responding? It needs to be demonstrated that similar behaviour could not be demonstrated with carbohydrate in general, artificial sweeteners or fat-rich palatable foods. Comparisons have been made between the reaction of rats to the provision of sucrose, a high-fat diet and a sweet-fat combination.<sup>7</sup> The ability of the opioid antagonist naloxone to produce withdrawal symptoms was

not observed with fat although it occurred when sucrose alone was provided, evidence that in this paradigm different types of palatable food produce different responses.

However, it appears that rats do not have a preference for sucrose consumption as there is a preference for sucrose in sham feeding studies, where after passing through the mouth it leaves the body, ensuring no post-ingestive effects occur. Dopamine is released from the nucleus accumbens with this procedure.<sup>8</sup> The sweetness of fruit juices is rewarding as judged by “reward expectation-related neuronal activity” in the primate striatum, although it is produced by sugars other than sucrose.<sup>9</sup> There is a preference for artificial sweeteners<sup>10</sup> that in turn have been shown to influence the activity of the nucleus accumbens.<sup>11</sup> The intermittent access of rats to a saccharin solution rather than sucrose has also resulted in withdrawal symptoms when consumption stopped.<sup>2</sup> It appears that in part at least there is a response not to sucrose but rather to a sweet taste. In contrast Hoebel<sup>2</sup> suggested that in his rat model of addiction there was probably a greater response to sucrose as there are specific receptors on the tongue and in the gut. The taste receptor type 1 member 3, encoded by the *TAS1R3* gene, responds to sweet tasting stimuli and is found in the gut as well as on the tongue.

More generally, is the response of a rat specifically to sweetness rather than palatability? Woolley<sup>12</sup> questioned whether the opioid regulation of food consumption reflects the macronutrient content rather than flavour. They studied the consumption of two types of food pellets that differed in flavour although they were nutritionally identical. A  $\mu$ -opioid receptor agonist injected into the nucleus accumbens increased the consumption of both pellets in a similar manner if they were tested when only one of the two foods was present. However, when both flavours of pellets were presented simultaneously, the agonist increased and the antagonist naltrexone selectively decreased, the consumption of the preferred flavour. The authors suggested that based exclusively on flavour cues, opioid mechanisms in the nucleus accumbens increase the intake of palatable foods. Similarly the administration of naltrexone into the nucleus accumbens selectively decreased sucrose intake, although it had only a minimal influence on the consumption of less preferred chow.<sup>13</sup> In addition a specific  $\mu$ -agonist selectively increased the intake of sucrose, saccharin and a dilute saline solution.<sup>14</sup> These findings demonstrated an important role for opioids in the nucleus accumbens in promoting the consumption of preferred palatable foods. When rats consumed a high-palatability sucrose solution the release of dopamine in the nucleus accumbens was dose dependent<sup>15</sup> but palatable high-fat/sweet foods similarly induced dopamine release.<sup>16</sup> The message is that it is palatability rather than sweetness or being sucrose that is critical in determining food preference.

This conclusion is supported by studying the impact of opioid drugs. As a generalization it has been known for many years that opioid agents enhance and opioid antagonists decrease feeding. In the rat the positive facial response to a sucrose solution was enhanced by morphine<sup>17</sup> and decreased by opioid antagonists.<sup>18</sup> The administration of morphine caused a short-term increase in food intake, and at least initially an increase in fat intake at the expense of carbohydrate.<sup>19</sup> The opioid antagonist, naloxone, decreased fat rather than carbohydrate consumption in rats.<sup>20,21</sup> As it is known that for many rats fat is more attractive than carbohydrates these findings are consistent with the view that opioid mechanisms influence the intake of palatable foods. Such a suggestion is supported by the study of initial food preferences. As there is variability amongst rats in their preferences for carbohydrate and fat, Gosnell<sup>22</sup> considered whether morphine was acting on food preferences. They distinguished fat-preferring from carbohydrate-preferring rats. Morphine increased carbohydrate

intake in carbohydrate-preferring rats and increased fat intake in fat-preferring rats. Therefore morphine increased the intake of the preferred diet rather than a specific macronutrient. Similarly naloxone selectively decreased the intake of preferred foods and not sucrose content as would be predicted by the ‘sugar addiction’ hypothesis.<sup>23</sup>

## 2. Sugar and reward mechanisms

### Summary

- Addictive drugs and palatable food both release dopamine from the nucleus accumbens.
- The nucleus accumbens has different populations of neurones that are activated by natural and drug reinforcement. The release of dopamine by natural rewards, unlike drugs of abuse, undergoes rapid habituation.
- Although the food-induced release of dopamine is markedly inhibited by pre-exposure to visual and olfactory stimuli that have been conditioned to food, similar visual and olfactory stimuli that had previously been conditioned to drugs of abuse strongly potentiate the dopaminergic reaction.
- The suggestion, based on the animal evidence, is not that palatable foods are physically addictive but rather that a particular style of eating can produce a reaction to food that is similar to the response to drugs of abuse.

### 2.1. Introduction

Central to the suggestion that sugar can be addictive is its interaction with reward mechanisms in the brain. Evolution could not anticipate the use of drugs of abuse so it is inevitable that such substances stimulate existing neural circuitry. Frequently it is suggested that drugs act at the sites that developed during evolution to react to natural rewards such as food, drink and sex.<sup>24,25</sup> The pathway that is stimulated by natural rewards is associated with the median forebrain bundle (MFB): the nucleus accumbens (NA), the ventral tegmental area (VTA), the ventromedial and lateral nuclei of the hypothalamus and the amygdalae.<sup>26,27</sup>

The MFB is a tract of neurones with cell bodies in the midbrain and synaptic terminals in the nucleus accumbens. The nucleus accumbens and ventral tegmental areas have been particularly implicated in mediating the action of drugs of abuse. The orbitofrontal cortex is also important for the processing of rewards. Based on neuroimaging studies<sup>28</sup> it was proposed that medial orbitofrontal cortex activity was associated with monitoring the reward value of a range of different reinforcers. For example it was reported<sup>29</sup> that sucrose consumption rather than water activated the right posterior orbitofrontal lobe. In food deprived subjects the presentation of food significantly increased metabolism in the whole brain but, in particular, the increased activity of the right orbitofrontal cortex correlated significantly with increased reports of hunger and the desire for food.<sup>30</sup>

It has been proposed that there are different aspects to reward<sup>31</sup>: liking, a pleasant experience, and wanting (incentive salience) that is the motivation to seek out the reward. In terms of neurobiology it is possible to distinguish wanting and liking although they are often occur experienced together. Many of the neurones that form the MFB release the neurotransmitter dopamine that is thought to be associated with ‘wanting’<sup>32</sup>; such that it is released in anticipation of a natural reward but not after it has been received.<sup>33</sup> The administration of drugs that block the action of dopamine at the nucleus accumbens produce animals that will consume food but will not seek it out. Without a functioning nucleus accumbens or MFB an animal will not work to obtain

a reward. The critical role played by this mechanism in food intake is illustrated by the fact that animals with lesions to these mechanisms will die as they do not eat or drink unless food and water is artificially given by a tube into the stomach.<sup>34,35</sup> Conversely drugs that increase the activity of dopamine in the nucleus accumbens increased the work that rats are prepared to perform to gain access to sucrose, although it does not increase the amount consumed or 'liking' as judged by facial expression.<sup>31</sup>

Berridge<sup>36</sup> stressed that the word wanting when used as a shorthand for incentive salience differs from the way that the word is used in everyday language. The ordinary sense of the word implies that there is an explicit goal associated with a conscious subjective feeling. These are very cognitive processes: "involving declarative memories of the valued goal, explicit predictions for the potential future based on these memories, and cognitive understanding of causal relationships that exist between your potential actions and future attainment of your goal." In contrast in the incentive salience sense none of these cognitive processes need to be present and it can occur without conscious awareness. It is possible to 'want' something that is not cognitively wanted and is not even liked. The incentive-sensitization theory of addiction<sup>32</sup> suggests that sensitized wanting may explain why addictions are motivationally compulsive and long-lasting.

If dopamine mediates wanting then which neurones modulate liking? Sites in the nucleus accumbens and ventral pallidum, but also parabrachial nucleus in the pons have been implicated in liking palatable foods.<sup>36</sup> Opioid mechanisms have been implicated with neurones of the MFB bundle releasing opioids. The injection of endorphins into the nucleus accumbens of a rat increases the 'face liking' response to sucrose.<sup>35</sup> In humans drugs that block the action of endorphins decrease the reported enjoyment of food.<sup>37</sup> The pleasantness of foods is not uniformly affected with sweetened, fatty, and high-protein foods being most influenced.

Berridge<sup>36</sup> considered the role played in the aetiology of eating disorders by motivational 'wanting' and the hedonic 'liking' and commented that "at present the data are ... still not entirely clear, and sometimes even a bit contradictory. Most fundamentally, there is still debate about whether food addictions really exist." He did not, however, exclude the possibility that the overeating of some individual might reflect the abnormal functioning of either the wanting or liking mechanisms although we await evidence.

## 2.2. Activation of reward circuits

One basis for the claim that sugar can be addictive<sup>1</sup> was the similarity between the effects of sugar and drugs of abuse on reward circuits. To evaluate the conclusions that can be drawn from such an analogy it is necessary to establish the normal functioning of these brain circuits. A review of the topic<sup>38</sup> concluded that the reinforcing effect of virtually all drugs of abuse is primarily dependent on activation of the mesolimbic dopamine system. There is also good evidence that sucrose increases the release of dopamine in the nucleus accumbens. For example in sham fed animals, where a sucrose solution entered the mouth but then left the body via a cannula, sucrose intake linearly increased dopamine release in the nucleus accumbens.<sup>8</sup>

However, the role played by such a reward needs to be placed in context as music,<sup>39</sup> humour,<sup>40</sup> winning<sup>41</sup> or expecting to win a prize,<sup>42</sup> attractive<sup>43,44</sup> or smiling faces,<sup>45</sup> a mother recognizing their child<sup>46</sup> or being in love<sup>47</sup> also stimulate these pathways. That such a wide range of pleasant phenomena activate these mechanisms suggests that rather than seeing the stimulation of these pathways by sucrose as something unusual or worrying, it can be viewed as one of a wide range of positive experiences that routinely stimulate a common circuitry. Thus a sucrose-induced release of

dopamine in reward pathways cannot be viewed as sufficient evidence that it is 'addictive': although if food was addictive dopamine would be released.

The critical question is whether highly palatable food has more in common with the many pleasurable normal and natural experiences that cause the release of dopamine, rather than drugs of abuse. It might be suggested that although evolution predisposed us to like sweetness, it did not prepare the body for the highly palatable foods that have been manufactured in more recent times. Have aspects of the modern diet more in common with drugs of abuse than the natural rewards that were available while the brain evolved?

## 2.3. Comparisons of dopamine release induced by food and drugs of abuse

Although addictive drugs and palatable food both increase the release of dopamine from the nucleus accumbens it appears that they influence different populations of neurones. Such a conclusion is supported by studies in which either pharmacological manipulation or selective lesions reduce the self-administration of cocaine but do not influence the response to natural rewards. For example Caine and Koob<sup>48</sup> used 6-hydroxydopamine to deplete the nucleus accumbens of dopamine and found a reduction in cocaine self-administration without altering the response to food.

Additional evidence arises from the study of the time scale of dopamine release. Dopaminergic functioning can be estimated using a range of methods. Recording the rate of firing of dopaminergic neurones allows the examination of functioning in a milli-second time frame. Similarly voltammetry measures dopamine release over sub-second periods. In contrast, microdialysis is used to estimate extra-cellular concentrations of dopamine over longer periods.

### 2.3.1. Neurophysiology

Carelli<sup>49</sup> reviewed studies that have examined electrophysiological activity in the nucleus accumbens within seconds of lever pressing for cocaine, water or food reinforcement. The majority of neurones tested exhibited similar patterns of neuronal firing with both food (not necessarily sucrose) and water. In contrast, most neurones displayed different patterns of firing with cocaine reinforcement. Carelli<sup>50</sup> concluded that "cocaine activates a neural circuit in the nucleus accumbens that is largely separate from the circuit that processes information about food and water reward." Similarly in monkeys<sup>51</sup> different neuronal pathways responded to cocaine and juice rewards. It was not possible to predict the neuronal response to one type of reward from the response to the other. It was concluded that the: "mechanisms by which cocaine acts do not appear to be the same as the ones activated when the monkeys were presented with an oral juice reward."

It appears that neurones in the nucleus accumbens respond differently to 'natural' reinforcers and cocaine. The data are consistent with the suggestion that the nucleus accumbens is a collection of groups of cells where different populations of neurones are activated by natural and drug reinforcement.<sup>52</sup> These findings are consistent with the suggestion that at least under normal conditions of consumption sucrose acts on different brain circuits to drugs of abuse. Such findings do not, however, preclude the possibility that animals kept under the conditions of the Hoebel<sup>1,2</sup> paradigm might not react in a different way to those consuming sucrose in a more usual manner.

### 2.3.2. Voltammetry

The use of fast-scan cyclic voltammetry, to measure dopamine released every 100 milli-second by the nucleus accumbens, found

that it was released prior to but not during sucrose consumption.<sup>15</sup> In contrast, although dopamine release occurred immediately prior to the consumption of cocaine, it was also released for the one to two seconds after consumption.<sup>53</sup> Such data are consistent with an inherent difference between drugs and natural reinforcers. Roitman et al.<sup>54</sup> concluded: "...where these data differ, however, is that dopamine quickly returned to baseline levels after the operant response for sucrose, but there was another rise in dopamine for cocaine." Similarly Di Chiara<sup>55</sup> observed that: "Drugs share with non-drug rewards the property of stimulating dopamine transmission in the nucleus accumbens shell but this effect does not undergo habituation upon repeated drug exposure, as is the case with non-drug rewards." These conclusions are based on studies of rats fed novel highly palatable foods. In animals who were not food deprived the feeding of an unfamiliar palatable salty food stimulated dopamine transmission in the nucleus accumbens, however, the effect was less when the procedure was repeated the next day, that is the dopamine response had habituated.<sup>56</sup> The habituation of the dopamine response in the nucleus accumbens disappeared completely after five days when the rat had not been exposed to the novel food. In a later study the release of dopamine stimulated by chocolate was also less when it was consumed for a second time. The reduced dopamine response was specific; there was no cross-tolerance between two palatable foods that had different tastes.<sup>57</sup>

### 2.3.3. Microdialysis

The release of dopamine from the nucleus accumbens is associated with both feeding<sup>58,59</sup> and the self-administration of cocaine.<sup>60,61</sup> However, as estimated by microdialysis, although palatable food and drugs of abuse both stimulate dopamine transmission in the nucleus accumbens, the nature of adaptation to these two types of reward differs. Di Chiara<sup>62</sup> listed three ways in which the reaction to food and the reaction to drugs of abuse differ. After a single trial the dopamine response to food decreases and this inhibition of dopamine release is only slowly reversed. In contrast the dopaminergic response to drugs of abuse is resistant to habituation, the release of dopamine continues. It is possible that this rapid habituation of dopamine release from the nucleus accumbens when consuming palatable food parallels the rapid sensory specific satiety that occurs during a meal. A sweet, savoury or other taste rapidly loses its attraction although you still are prepared to consume differently flavoured food. Ahn and Phillips<sup>63</sup> supported this view. Although rats consumed an initial palatable food they ate little when it was produced as a second meal. However, if given a different palatable food they ate a significant quantity as a second meal. The release of dopamine paralleled the presentation and consumption of novel palatable foods. Thus a food tended to stimulate dopamine release when it was both novel and palatable.

Secondly while the food-induced release of dopamine was markedly inhibited by pre-exposure to visual and olfactory stimuli that had been conditioned to food, similar visual and olfactory stimuli that had previously been conditioned to drugs of abuse strongly potentiated the dopaminergic reaction to the drug.<sup>62</sup> Thirdly food-conditioned stimuli were found to stimulate the release of dopamine in the pre-frontal cortex but not the nucleus accumbens. In contrast, drug-related stimuli stimulated dopamine release in both the pre-frontal area and the nucleus accumbens: there appears to be a basic difference between food and drugs of abuse. The dopaminergic response of the nucleus accumbens decreased when exposed to food-conditioned stimuli, whereas drug conditioned stimuli had the opposite effect and they increased the release of dopamine. Di Chiara and Bassareo<sup>64</sup> noted that by acting directly on the brain, drugs of abuse bypass the adaptive mechanisms (habituation) that occur with food rewards that

inhibit the responsiveness of the nucleus accumbens. With drugs of abuse it is the lack of habituation of the dopamine response that characterizes addiction; in this way the abnormal motivational learning and the conditioning of drug-related stimuli develop. The pattern of dopamine release also differs. Whereas food-conditioned stimuli release dopamine from the core but not the shell of the nucleus accumbens, drug conditioned stimuli release dopamine from the shell but not core.<sup>62</sup> This difference is significant as it allows the acquisition of excessive incentive-motivational properties by drug conditioned stimuli that are intrinsic to drug addiction.

Fallon<sup>65</sup> measured three neurotransmitters in eight brain areas of rats after feeding and found a pattern of changes different to those associated with either nicotine or cocaine. They concluded that the "reward response is highly dependent on the substance tested, demonstrating that multiple reward mechanisms operate which can encode for different stimuli". You need more than a simple measure of dopamine release to demonstrate a homology between food and drugs of abuse. The timing scale of the release, the conditions under which the release occurs and the pattern of changes in different areas of the brain need to be considered. In the rat following a normal feeding schedule the nature of the food-induced stimulation of reward pathways differs from drugs of abuse. Avena et al.<sup>1</sup> acknowledged this when they noted that "normal feeding is very different than taking drugs because the dopamine response during feeding phases out." In contrast: "rats fed daily intermittent sucrose and chow apparently release dopamine every day". Thus the stimulation of the release of dopamine from the nucleus accumbens of rats maintained under the regime of Avena et al.<sup>1</sup> fails to habituate in a way that occurs with a typical feeding regime. The question is whether the reaction of rats to normal feeding is more typical of human feeding, than the reaction of rats kept under an unusual feeding schedule?

Thus the physiological evidence gives little support to the suggestion that the normal consumption of palatable food is mediated by a mechanism similar to that underlying drug addiction. Although it is generally agreed that palatable food is not addictive the possibility remains that the way in which it is consumed might be influential, specifically if it is consumed intermittently as a binge. The claim that needs to be considered, is not whether sugar is intrinsically physically addictive, but rather whether some humans consume it in a manner that produces addiction?

## 3. Is sugar addictive in humans?

### Summary

- If physical addiction plays a role in the consumption of sugar then various phenomena associated with addiction, for example craving and tolerance, would be predicted to be observed.
- Most people experience food cravings at one time or another, most commonly for items high in fat or containing a mixture of fat and sugar.
- Fasting leads to a decline in craving and not an increase as the addiction model predicts.
- Food cravings occur to a greater extent later in the day while the addiction model predicts, as occurs with drugs of abuse, that they should also occur early in the morning.
- Food craving, particularly for chocolate, occurs more towards the end of the menstrual cycle, whereas the menstrual cycle does not influence the reaction to drugs of abuse.
- Exposure to sweet tastes may increase food preference although the phenomenon is associated with a particular form of a particular food. Rather than tolerance it is probable that we develop expectations about the taste of specific food items.

- Children like intensely sweet tastes, a preference that declines during adolescence, a finding inconsistent with the development of tolerance.

### 3.1. Food craving

The possibility that sucrose consumption is generally associated with characteristics of physical addiction is discussed initially before specifically considering eating disorders.

Although Tiffany<sup>66</sup> proposed that drug use is largely controlled by automatic processes, cravings play a part when intake is prevented, and in relapse following periods of abstinence. If addiction was an important mechanism that underlies the intake of sucrose, then cravings would be predicted to play a role. Pelchat et al.<sup>67</sup> reported the first imaging study of food craving. Subjects imagined either the sensory properties of their favourite foods or a non-craved monotonous diet. Cravings were associated with activation of the hippocampus, insula and caudate, three areas reported to be involved in drug craving.<sup>67</sup> Thus it appeared that food and drug craving may be mediated by a common neural substrate. Of itself this finding does not demonstrate that food craving is pathological, as one theory is that food cravings are a means of ensuring a varied diet. Hence drug craving may reflect the abnormal stimulation of mechanisms that evolved to encourage a balanced diet.

Physical dependence and associated withdrawal symptoms were once believed to be the key features of addiction to drugs of abuse. It is now realised that this is not the case as cravings, resulting in relapse, can occur months or years after withdrawal symptoms have disappeared. Thus a sugar addiction model predicts that, by analogy to drugs of abuse, sugar cravings should develop when consumption is limited. Ninety-seven percent of woman and sixty-eight percent of men reported experiencing food cravings: thirty-nine percent of women reporting chocolate cravings compared with fourteen percent of men.<sup>68</sup> The most craved food for men was not sweet, it was pizza. Hill<sup>69</sup> reviewed the topic and concluded that “food cravings are extremely common, reported by the majority of young adults. They are closely associated with liking but not synonymous with increased intake.” Food cravings are most commonly reported for either savoury/salty foods or sweet/fatty emulsions such that the texture and mouth feel are important. There was no reported craving for sweetness as such, for example craving for sweetened carbonated drinks did not appear on the list of Weingarten and Elston.<sup>68</sup>

As chocolate is the most craved food item an examination of the underlying motivation will help to establish the viability of the addiction hypothesis Benton et al.<sup>70</sup> offered a detailed examination of the reaction to chocolate consumption. The major underlying dimension was labelled craving and was associated with a considerable preoccupation with and liking the taste and mouth-feel of chocolate. Interestingly this dimension was not associated with withdrawal but rather consumption when under emotional stress. It was eaten when bored, upset or feeling low. There was a link between negative mood and the desire to consume chocolate: it was ‘comfort eating.’ The experience of strong food cravings has been associated with being bored, anxious and having a dysphoric mood<sup>71</sup> rather than having avoided eating the food item for a period of time.

#### 3.1.1. The dimensions of food craving

White<sup>72</sup> developed the Food-Craving Inventory, a self-report measure of food cravings. Subjects were asked the frequency with which they craved forty-seven foods. Four groups of craved foods resulted: high fats (fried chicken, hot dogs, sausage, and steak); sweets (cookies, candy, brownies, chocolate, and cake); carbohydrates/starches (potato, pasta, rice, and bread); fast-food fats

(hamburger, French fries, chips (crisps), and pizza). This approach places craving for sweetness in context as only eight of the foods weighted on the ‘Sweet’ factor. It is clear that sweet items are by no means the only items craved. In addition the sweet factor would be better labelled as sweet/fatty foods as they are characterized by a combination of fat and sugar, rather than sugar alone. Based on six examples of each type of sweet foods that were craved, the energy from cookies was calculated to be 37% from fat and 25% from sugar. The comparable data for brownies were 32% from fat and 26% from sugar; chocolate 45% fat and 48% sugar; cake 48% fat and 26% sugar; ice-cream 45% fat and 43% sugar. Only candy was predominantly sugar. Thus, with three of the four groupings of foods that were craved, fat was the predominant source of energy.<sup>72</sup> The exception was the carbohydrate/starch group although sugar was not associated with these foods. The impression created is that foods that are craved tend to be high in fat rather than high in sugar, albeit in one grouping high levels of sugar and fat were associated. This observation is supported by Pelchat<sup>73</sup> who found that: “The majority of foods craved were high in fat. Indeed, only 11 (e.g. plain fruit or vegetables) out of 192 were fat free”. In a sample with the mean age of 44 years, with both males and females, items in the carbohydrate group (that did not include sweet items) were most commonly craved.<sup>74</sup> In males craving for carbohydrate was significantly more common than craving for sweet/fatty items. In fact in males sweet/fatty foods were the least craved although females reported craving sweet/fatty substances more frequently than males.

#### 3.1.2. Fasting

Although folklore suggests that fasting leads to food craving, it is not a view that is supported by the literature. Lappalainen<sup>75</sup> asked a group who were fasting to report food cravings for three-weeks. Fasting almost completely abolished reports of craving. Harvey<sup>76</sup> also found significant decreases in cravings for all types of foods over the twenty weeks during which a group of obese patients dieted. Similarly Martin<sup>77</sup> examined food cravings over twelve weeks in obese patients who consumed either a low-calorie or very low-calorie diet. The reports of craving decreased rather than increased with dieting, and to a greater extent in those eating the more restricted diet. It appears that food cravings diminish with calorie restriction, rather than increasing as an addiction model predicts.

If food addiction is a major mechanism leading to obesity then it must drive food intake on a regular basis. It is relevant that Pelchat<sup>73</sup> asked her subjects to describe their experience of food cravings over the previous year and not a shorter period. Hill<sup>71</sup> reported that those who experienced food cravings had them two to four times a week. Martin<sup>77</sup> asked a group of the obese to put the frequency of food cravings on a five point scale. The baseline ratings for craving sweet/fatty items was 2.25; where a rating of three was sometimes, and two represented being rarely experienced. With fasting, ratings fell to an average of 1.25 where a rating of one represented being never experienced. Even the highest baseline rating was only 2.5 for fatty fast foods.

The message is that food cravings do not occur regularly enough to explain habitual food intake. The relative infrequency of food cravings contrasts with the daily need to obtain drugs of abuse by those who are addicted. As we eat several times a day, if obesity was driven by food addiction, you would expect craving to occur more frequently. The relatively infrequent nature of food cravings, especially after abstinence, suggests that they are not a major factor in day to day food choice.

#### 3.1.3. Factors influencing craving

A strong relationship has been reported between the craving for chocolate and sweet foods and the stage of the menstrual cycle:

cravings increase towards the end of the cycle.<sup>78,79</sup> Turner and de Wit<sup>80</sup> reviewed the influence of the stage of the menstrual cycle on the reaction to drugs of abuse. In contrast to chocolate they concluded that in general “ovarian hormones have modest, if any, effects on responses to abused drugs.” Cravings for nicotine are noticeable first thing in the day<sup>81</sup> and similarly alcohol dependent patients are more likely to start drinking in the morning.<sup>82</sup> This is the pattern that is predicted by an addiction model and the associated development of overnight withdrawal symptoms. In contrast Pelchat<sup>73</sup> found that food cravings were not evenly distributed throughout the day but tended to occur in the late afternoon and early evening. Although if an overnight fast was followed by fasting throughout the day then cravings would be expected in the evening, this is not the usual pattern of eating. Thus the factors that determine food cravings are not those that an addiction model predicts should be influential.

### 3.2. Changes in sucrose preference over time

Another characteristic predicted by the ‘sugar addiction’ hypothesis is that tolerance should develop: that is over time to obtain the same intensity of effect an increased dose must be consumed. In the absence of any obvious withdrawal symptoms, or behavioural or cognitive measure of the response to sucrose consumption, the topic can only be considered indirectly.

Giving sugar to a baby has a marked calming influence such that drinking a sucrose solution prior to the collection of blood reduced crying by fifty percent and similarly sucrose consumption decreased the expression of distress during circumcision.<sup>83</sup> Indirect evidence that the effect of this sweet taste was mediated by an opioid response is supplied by babies who were born to opiate addicted mothers in whom the calming effect of sucrose was reduced.<sup>84</sup> Although an opioid mechanism is implicated there is, however, no suggestion of addiction, as although the calming influence of sucrose can be demonstrated at birth the effect decreases over the first six weeks.<sup>85</sup>

Drewnowski<sup>86</sup> argued that given the difficulty in assessing sucrose intake you can consider the preference for sweetness as an index of potential food consumption. It is assumed that the acceptability of a given level of sweetness influences the consumption of sucrose.

Experimental evidence that a child’s experience of food will influence his or her preferences was reported by Liem and de Graaf.<sup>87</sup> They gave orange drinks with either a sweet or sour taste that were equally preferred at baseline. After an eight day exposure to the sweet drink preference for this drink increased significantly, although exposure to the sour drink did not affect preference. Beauchamp and Moran<sup>88</sup> found children who had been fed sugar water regularly by their mothers consumed more sucrose solution compared with those who had not been fed sweetened water. However, this prior consumption of sucrose did not influence the consumption of a sweetened or unsweetened fruit-flavoured drink: the effects of exposure to sucrose were specific to the medium in which sucrose was dissolved. Similarly Sullivan and Birch<sup>89</sup> found that by six months of age children fed sweetened water preferred it. However, pre-school children given sweetened, salty or plain tofu preferred the type with which they were familiar, indicating there was no general increase in the desire for sweetness, but rather a preference for the flavour normally associated with the food item.

Rather than seeing such phenomena as evidence of tolerance a more probable explanation is that as we eat novel foods we rapidly develop expectations about taste and texture,<sup>90</sup> such that when we next eat a food item any deviation from this norm is viewed negatively. An everyday example will illustrate the phenomenon. Some people like sucrose added to hot tea or coffee

whereas others do not. For example a child, who has been used to adding sugar to their drinks, might decide as an adult to stop the practice. Initially the unsweetened drink will taste unpleasant but rapidly it will become acceptable to the extent that a sweetened drink will be now taste unpleasant. The key matter is the expectation of how the food will taste. Thus although there is a genetically determined liking for sweetness a change in the preference over time does not necessarily demonstrate tolerance.

Evidence suggesting that tolerance does not occur comes from the study of changes in preferences over age. The addiction model predicts that as tolerance develops there should be an increase in intake to achieve the same reaction. Humans are born with a preference for a sweet taste,<sup>91,92</sup> however, although the preference for intense sweet tastes remains during childhood, it declines during adolescence so that the adult has a preference for moderate rather than high sweetness. Desor and Beauchamp<sup>93</sup> measured preferences for the taste of sucrose in a sample aged eleven to fifteen years, and again when the same subjects were nineteen to twenty-five years. They found that the preferred level of sweetness decreased from childhood to being a young adult. Zandstra and De Graaf<sup>94</sup> considered preferences for different concentrations of sucrose in those aged from six to over sixty-five years. Those from six to twelve years of age, compared with those who were older, found that all concentrations of sucrose were more pleasant. Whereas children liked stronger concentrations of sucrose, adults found the two highest concentrations (18.1% and 23.5% w/w) less pleasant than lower concentrations. Similarly those aged nine to fifteen years of age preferred greater sweetness and saltiness than adults.<sup>95</sup> The most preferred concentration for the younger group was 20% sucrose w/w, compared with only 5% w/w in adults. This decline in the preferred concentration of sucrose with age is opposite to that predicted by the addiction hypothesis. A plausible suggestion is that in rapidly growing children genetic predispositions favour the intake of high sources of energy, a need that has declined by adulthood. There are, however, in addition genetically determined individual differences in the response to sweetness; some prefer sucrose of increasing concentrations whereas others dislike high concentrations. In both children and adults the liking of very sweet items tends to be associated with a genetically determined inability to taste 6-n-propylthiouracil (PROP). In contrast those who dislike very sweet items tend to be able to taste PROP.<sup>96</sup>

Much is still unknown about the reaction to drugs of abuse. A potentially confusing topic, to those more familiar with drug tolerance, is behavioural sensitization (reverse tolerance). This occurs when repeated and intermittent administration results in an increased response to a drug. The incentive-sensitization theory suggests that addiction is caused primarily by drug-induced sensitization in the brain mesocorticolimbic systems, so that stimuli associated with reward gain increased “incentive salience” resulting in enhanced motivation (wanting) for drugs.<sup>97</sup>

There have been isolated suggestions that food can have a similar influence. Le Merrer and Stephens<sup>98</sup> gave novel sweetened pellets to mice and measured locomotor activity on a runway that increased with repeated testing, something that did not occur when the food was eaten in the home cage. This conditioned activity was reduced by the opiate antagonist naltrexone and a dopamine D<sub>1</sub> antagonist. In addition naltrexone at doses that suppressed conditioned activity also suppressed cross-sensitization to cocaine. They concluded that “many of the features of behavioural sensitization to drugs can be demonstrated using food reward and may contribute to excessive eating”. These findings must be viewed with caution as previously no sensitization was found when the activity of rats was monitored following exposure to chocolate,<sup>99</sup> although the pairing of environmental cues with access to chocolate produced gene expression similar to that elicited by drug cues.

### 3.3. Sucrose, sweetness or palatability?

The idea that addiction can develop to a single food ingredient, sucrose, needs to be considered. Levine et al.<sup>100</sup> commented that: “The concept of macro-nutrient preferences is not concordant with human studies. Humans rarely request pure sugar or pure fat; instead they select foods such as candy or ice-cream ... humans react to the taste and texture of foods rather than their chemical content.” If a preference for a particular macronutrient is inconsistent with the literature is it reasonable to suggest a preference for one form of a macronutrient, sucrose?

#### 3.3.1. Palatability

Lowe and Butryn<sup>101</sup> noted: “As the growing prevalence of global obesity suggests, an increasing proportion of human food consumption appears to be driven by pleasure, not just by the need for calories.” They proposed a distinction between homeostatic and hedonic eating. The taste, texture and appearance of food influence the amount eaten. For example in a laboratory study Yeomans<sup>102</sup> studied the consumption of pasta with a sauce that varied in palatability. Both the amount consumed and the speed with which it was eaten was greatest with the most palatable meal. He suggested that palatability increases food intake by means of a positive-feedback reward mechanism with the release of opioids being part of this mechanism.<sup>103</sup>

de Castro<sup>104</sup> examined seven day dietary diaries and related these to ratings of palatability. Most meals that had been self-selected were palatable and the meals rated as most palatability were forty-four percent larger than those low in palatability. Palatability has a major impact on food choice and the amount eaten. Interestingly they commented that: “palatability appeared to be related more to the subjective state of the individual than to the composition of the meal.” Regression equations were calculated to predict palatability ratings. The macronutrient composition of the meal had only a weak relationship with palatability ratings. Time was influential as palatability ratings were higher later in the day. However, by far the strongest predictors of palatability were ratings of hunger and elation. Such findings caution against assuming that food preference mainly reflects the nutritional composition of the food. However, it is frequently suggested that sweetness increases palatability, particularly when it is combined with fat.

Drewnowski and Greenwood<sup>105</sup> asked subjects to rate the pleasantness of various combinations of milk, cream, and sucrose. With increasing levels of sucrose preference ratings rose and then declined; it was possible for the mixture to be too sweet. In contrast hedonic ratings continued to increase with higher amounts of dairy fat. Importantly the addition of sucrose increased the liking for high-fat stimuli. Fat gives food a pleasant mouth feel and carries flavour well. These findings indicated that the presence of too much sucrose can be unpleasant, although if it increases the preference for sweet/fatty items then the consumption of energy-dense foods may be encouraged.

In conclusion the study of food craving or the preference for a sweet taste gives no support to the hypothesis that food intake, or more specifically sucrose consumption, reflects addiction.

## 4. Sugar consumption and obesity

### Summary

- Energy-dense diets play a causal role in causing obesity.
- The fat and water content of food, rather than sucrose intake, are the primary determinants of energy density.

### 4.1. Introduction

If an addiction to sucrose is a major determinant of body weight it is reasonable to expect an association between its consumption and the incidence of obesity. Although many years ago there was a tendency to believe that a high carbohydrate intake was associated with obesity, since the 1990s more attention has been directed to the intake of fat. A ‘sugar-fat seesaw’ has been discussed as a diet low in fat tends to be high in sugar and vice versa. Hill and Prentice<sup>106</sup> commented that “Metabolic studies show that diets high in fat are more likely to result in body fat accumulation than are diets high in carbohydrate. There is no indication that simple sugars differ from complex sugars in this regard. Epidemiologic data show a clear inverse relation between intake of sugar and fat. Further, although high intake of dietary fat is positively associated with indexes of obesity, high intake of sugar is negatively associated with indexes of obesity. There is ample reason to associate high-fat diets with obesity but, at present, no reason to associate high-sugar diets with obesity.”

The recent tendency has been to concentrate on the energy density of the diet<sup>107,108</sup>; that is the amount of available energy per weight of food (kJ/g). As we tend to eat a relatively constant amount of food the number of calories provided by a given weight of food is critical. The major factors that determine energy density are water and fat content, to the extent that these account for 99% of the variance, with water content having the greater influence.<sup>109</sup> The WHO Report<sup>110</sup> concluded that there was “convincing evidence” that a high intake of energy-dense foods is associated with an increased risk of obesity. However, the sucrose content of food plays virtually no role in the determination of energy density.

### 4.2. A sweet-tooth?

Drewnowski<sup>86</sup> considered the ‘sweet-tooth’ hypothesis; that the obese find intensely sweet foods attractive. This suggestion was supported by early work,<sup>111</sup> although a series of subsequent studies either found no relationship or that the obese preferred less sweet items.<sup>112,113</sup> A related approach is to look for individual differences in changes in preference with an increasing concentration of sucrose. Thompson<sup>113</sup> distinguished a Type I response that was an inverted-U in which preferences increased to an optimal sucrose concentration after which they declined. With a Type II response preference increased with concentration until a plateau was reached after which preference remained constant. Most obese were Type I, that is higher concentrations of sucrose were less preferred. Subsequently the idea of the sweet-tooth was modified to suggest a preference for energy-dense foods that were high in fat, or fat and sugar.

### 4.3. Dopamine and obesity

The demonstration that the involvement of striatal dopamine mechanisms differs in those who are obese has been used to support the suggestion that the palatability of foods plays a critical role in weight gain. There are, however, no straightforward conclusions to be drawn. The work of Norma Volkov has drawn parallels between the neurological responses to drugs of abuse and obesity, with the suggestion that as dopamine also modulates the rewarding properties of food it is likely to be involved in overeating. When the availability of striatal dopamine D<sub>2</sub> receptors in brain was measured using positron emission tomography they were lower in the obese. Importantly, “the availability of the dopamine D<sub>2</sub> receptor was decreased in obese individuals in proportion to their BMI”.<sup>114</sup> As low levels of dopamine D<sub>2</sub> receptors have also been found in individuals addicted to a variety of drugs it was

hypothesized that the decrements in dopamine D<sub>2</sub> receptors in the obese reflected down regulation, a compensation for a feeding-induced increase in dopamine release.

These brain imaging studies are difficult to interpret as the correlations they have produced cannot establish causal mechanisms. When recruiting somebody to a study relating to eating do the reactions to pictures of food reflect the food as such, rather than pre-existing expectations that may in part result from societal attitudes rather than the nutritional properties? It is also impossible to say whether the lowered levels of dopamine receptors predated pathological eating and therefore played a role in its development, as opposed to being a consequence of what was eaten.

Comings and Blum<sup>115</sup> proposed a 'Reward Deficiency Syndrome' and suggested that the gene for the dopamine D<sub>2</sub> receptor was likely to play a role as the Taq 1 A1 allele of the DRD2 gene has been associated with alcoholism, drug abuse, smoking, obesity and compulsive gambling. It is interesting that Comings<sup>116</sup> found an association between a higher Body Mass Index and the presence of the DRD2 Taq 1 A1 allele although it should be remembered that there is polygenic inheritance.<sup>117</sup> Consistent with the view that pre-existing factors influence eating is that obese individuals with a binge-eating disorder are more likely to have a family history of substance abuse.<sup>118</sup> Thus imaging studies of those with different polymorphisms would be instructive as it is possible that rather than being a reflection of diet, in some individuals differences in dopaminergic functioning predate obesity.

Studies of the effect of the sight of food suggest that you do not need to eat food to stimulate the reward mechanisms. When shown pictures of appetising (e.g. cream cakes) or bland food (e.g. rice) the brain's response differed in those with a tendency to overeat<sup>119</sup>: brain areas associated with reward were more activated and the connections between brain regions were less apparent. Personality was also influential as those who displayed a tendency for greater 'external eating' (that is they react more to the sight and smell of food) responded more to appetising items. They also concluded that those with less efficient connections between relevant brain regions might result in a vulnerability to overeating.<sup>119</sup> The possibility arises that pre-existing differences in the wiring of brain predisposes to overeating.

Such findings also demonstrate that as the brains reward mechanisms respond to the sight of palatable foods and there is no need for sucrose, for example, to be consumed for reward mechanisms to be stimulated. Stoeckel<sup>120</sup> found that pictures of high rather than low caloric foods to a greater extent activated the reward areas of those who were obese. Also in obese individuals there was evidence of abnormal interactions between the ventral striatum, amygdala, anterior cingulate and premotor cortex areas. In the obese there was a failure to gain the appropriate emotional information that is needed to devalue a food following its consumption, resulting in increased weight.<sup>121</sup> Again we need to establish whether such differences in brain functioning predate obesity.

However, if the differences in dopamine activity post-dated an eating pattern then the neural changes might be pathological if they help to maintain overeating, or alternatively they might be a positive response if there was an attempt to down regulate over-stimulated mechanisms. Even if these differences in neural activity reflected the nature of the diet, when discussing the plausibility of sugar addiction imaging data have limited relevance unless obesity can be shown to be particularly associated with sucrose intake. This topic was discussed above but inevitably the obese will consume a diet containing a wide range of food items and associated nutrients. It is likely that palatable foods are consumed rather than sweet items as such.

A final concern is that these imaging studies have often dealt with 'the obese' as if they are a homogeneous group. What is certain about the control of eating and the development of obesity is that it reflects many biological mechanisms as well as genetic, economic, social and psychological factors. It is reasonable to expect that obesity will turn out to be a generic term that covers many heterogeneous disorders. In fact imaging studies suggest that brain circuits that deal with memory, inhibition, reward and motivation differ in the obese: it follows that the common outcome of obesity can potentially reflect a range of aetiologies.

In summary these imaging studies cannot distinguish whether differences in the brains of obese individuals are a consequence or a cause of the obesity. Further studies that assess D<sub>2</sub> receptors measures before and after successful weight reduction interventions might help determine if the low levels reflects changes secondary to the individual's high BMI.

## 5. Bingeing

### Summary

- The onset of Binge-Eating Disorder (BED) tends to occur in the mid-twenties at a time when a preference for a sweet taste has declined.
- Bingeing involves the consumption of a wide range of palatable foods not necessarily those that are sweet.
- There are a wide range of risk factors for eating disorders most of which are social and psychological rather than related to nutrition.
- The prediction from the rat addiction model, that dieting plays a critical role in the development of BED, was not supported by the literature.
- Opioid antagonists have a similar influence in those with BED as to the rest of the population. There was no evidence of the withdrawal symptoms predicted by the addiction hypothesis.

### 5.1. Introduction

The physiological (Section 2) and behavioural data (Section 3) suggested that palatable foods are not of themselves physically addictive. However, in rats it was possible to produce addiction-like behaviour by feeding sucrose in a highly prescribed manner.<sup>1</sup> Therefore the human literature will be considered to establish whether phenomena occur similar to those in rats 'addicted' to sugar.

Even if addiction to sucrose does not occur generally, is it possible that there are sub-groups of the population for which this food is a particular problem? Rogers and Smit<sup>122</sup> argued that binge eating has features that could reasonably lead to the label 'food addiction'. It is a pathological state in which there is a loss of control over eating, it is harmful to the individual and the attempt to gain control over eating is lost. However, this is no more than a verbal description of the outward signs of the disorder that of itself does not demonstrate the involvement of a biology shared with drugs of abuse. There are two basic possibilities. The first is that BED results directly from the diet consumed, in particular the pattern of sucrose intake.<sup>1</sup> The second possibility is that life events, other than the nature of the diet, create psychological problems to which binge eating becomes the 'psychological solution': that is bingeing and the composition of the diet is a symptom and not the cause of the problem. To allow the two possibilities to be distinguished relevant information must come from human studies, having initially examined the animal model to establish the features that are predicted to be critical.

In the paradigm of Hoebel<sup>1</sup> the dietary pattern of rats consisted of periods of fasting followed by access to standard laboratory chow

and an unlimited highly palatable sucrose solution. Superficial parallels exist with BED in which periods of dietary restraint are interspersed with eating to excess. If this is a homology an examination of the risk factors for BED should indicate an important if not predominant role for dietary factors. Predictions as to the nature of human binge eating, developed from the 'sugar addiction' hypothesis, are listed in Table 1. As in the rat model 'addiction-like' symptoms only developed when fasting occurred prior to an access to sucrose, a period of dieting, or at least a restricted food intake, would be predicted to predate the development of BED. There is no evidence that rats given continuous access to sucrose start to binge. The use of the term 'sugar addiction' implies that those with BED should display an unusually intense desire to consume sucrose. There is evidence that when rats binge on sucrose that opiate mechanisms are associated with the resulting addiction. Is there evidence in those with BED that there is a comparable involvement of opioid mechanisms?

## 5.2. Binge-eating disorder

BED has only recently become a recognized disorder that differs from bulimia nervosa in that bingeing is not followed by vomiting, the use of laxatives or excessive exercise. The Diagnostic and Statistical Manual of Mental Disorders<sup>123</sup> lists BED as a diagnosis requiring further study and presents the following diagnostic criteria:

- 1) Recurrent episodes of binge eating. An episode is characterized by:
  - a) Eating a larger amount of food than normal during a short period of time (within any two hour period)
  - b) Lack of control over eating during the binge episode (i.e. the feeling that one cannot stop eating).
- 2) Binge-eating episodes are associated with three or more of the following:
  - a) Eating until feeling uncomfortably full
  - b) Eating large amounts of food when not physically hungry
  - c) Eating much more rapidly than normal
  - d) Eating alone because you are embarrassed by how much you're eating
  - e) Feeling disgusted, depressed, or guilty after overeating
- 3) Marked distress regarding binge eating is present
- 4) Binge eating occurs, on average, at least 2 days a week for six months
- 5) The binge eating is not associated with the regular use of inappropriate compensatory behaviour (i.e. purging, excessive exercise, etc.) and does not occur exclusively during the course of bulimia nervosa or anorexia nervosa.

In the USA there is a lifetime prevalence of BED of three and a half percent in women and two percent in men, with an age of

onset of on average 25.4 years compared with about 19 years with both anorexia nervosa and bulimia nervosa.<sup>124</sup> Such demographic data give reason to begin to question a predominantly dietary explanation of the aetiology of BED. The vast majority of the American population regularly eat large amounts of sweetened foods, yet it is a small minority who develop the disorder, suggesting that other factors predominate. The relatively late age of onset again argues against a predominantly dietary explanation, as a preference for sweetness is greater in young children and declines markedly during adolescence<sup>91,92</sup> when the sugar addiction hypothesis predicts that it should increase. Given the greater attraction of sweetened foods in young children you would predict that the disorder would develop at an earlier age. A survey indicated the importance of factors other than diet.<sup>124</sup> They found fifty-one percent of those with BED had been treated for other emotional problems at some time in their life; data that suggests the possibility that the disorder may be an attempt to deal with a pre-existing psycho-pathology. One of the few long-term prospective studies found that elevated levels of perceived stress predated the onset of BED.<sup>125</sup>

Jacobi<sup>126</sup> reviewed factors that have been suggested to predispose to eating disorders and listed thirty, the majority of which were non-biological. They found that few of the putative risk factors preceded the onset of the disorder and others were general risk factors that did not distinguish between different types of eating disorders. Common risks associated with various types of eating pathology were gender, ethnicity, early childhood eating and gastrointestinal problems, concern about body weight and shape, poor self-esteem, sexual abuse and other stressful experiences, and a history of general psychiatric problems. The use of meta-analysis<sup>126</sup> offered more precise conclusions. There was consistent support for some of the previously less-accepted risk factors such as 'thin-ideal internalization' and negative affect, whereas social support was helpful. In contrast other accepted risk factors for eating pathology, for example sexual abuse, did not receive support.

The 'sugar addiction' model proposes that the consumption of large amounts of palatable foods causes the release of opioids in quantities sufficient to allow addiction to develop. In the rat model the critical sequences was fasting followed by bingeing; there is no evidence that rats with regular access to sucrose develop the changes in biology and behaviour that would lead to the suspicion that addiction occurs. The parallel was drawn with BED where dieting is followed by bingeing.<sup>1</sup> As the rat model relies on a period of fasting to induce 'addiction', if this is a homology of BED then a period of dieting should predispose to the development of BED.

Stice<sup>127</sup> considered the history of dieting prior to the development of BED and concluded that "dieting is not a risk factor for eating pathology." The National Task Force on the Prevention and Treatment of Obesity<sup>128</sup> reviewed the dieting literature and concluded that: "Moderate caloric (energy) restriction, in combination with behavioural weight loss treatment, does not seem to cause clinically significant binge eating in over-weight adults without preexisting binge-eating problems and might ameliorate binge eating, at least in the short term, in those reporting recurrent binge eating before treatment." Howard and Porzelius<sup>129</sup> found "that only a minority of individuals with BED report that dieting preceded the onset of binge eating.

As one example Goodrick<sup>130</sup> compared the effectiveness of non-dieting and dieting treatments for over-weight, binge-eating women. Dieting reduced binge-eating scores rather than increasing them as the addiction model predicts. Telch and Agras<sup>131</sup> similarly compared obese female subjects, half of whom were binge eaters, on a very low-calorie diet or a behavioural weight loss programme. The frequency of binge-eating episodes was similar while on the

**Table 1**

Characteristics of human who binge predicted from the putative rat model of eating disorders.

<p>There is a hypothesized parallel between 'sugar addiction' in rats and binge-eating disorder/bulimia nervosa in humans: both restrict food intake and binge later on palatable foods. If there is a homology then it is predicted that:</p> <ul style="list-style-type: none"> <li>• Dieting should predate the development of binge-eating disorders</li> <li>• Binge eating should develop at a younger age when there is a greater preference for sweetness</li> <li>• Sweet items should be preferentially consumed while bingeing</li> <li>• Opioid antagonists should cause withdrawal symptoms in those who binge</li> <li>• Opioid antagonists should increase bingeing in those with such disorders</li> <li>• An opioid antagonist should act at a dose that blocks opioid activity</li> </ul>
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diet, although in both binge and previously non-binge eaters, episodes of bingeing occurred after the reintroduction of a normal diet: a phase that had passed after three months. The stated reason for the study of Wadden<sup>132</sup> was the fear that dieting may precipitate binge eating and other adverse consequences in the obese even when there was no diagnosis of BED. Obese women were randomly assigned to one of two diets or a non-dieting approach. Over 65 weeks there were few differences in the incidence of reported bingeing. They advised that concern about adverse behavioural responses should not discourage the recommendation that the obese should restrict energy intake.

It seems that the prediction that dieting leads to binge eating is not supported by the evidence. It is more common for dieting to be a response to being over-weight than to predate the development of binge eating.

### 5.3. Foods eaten while bingeing

As the rat model predicts that bingeing reflects an addiction to sweet foods, an examination of the foods consumed while bingeing can be used to test the hypothesis. Is the assumption that it is sweet foods that are preferentially consumed while bingeing supported by the evidence?

Leon<sup>133</sup> found that the foods eaten during a binge fell into two main groups: Breads, pastries, biscuits (cookies) and other carbohydrates or alternatively potato crisps (chips) and pretzels. The only foods that distinguished bingeing from non-bingeing were these two types of food.<sup>134</sup> Similarly the occasional binges of non-bulimic students involved the consumption of these foods.<sup>135</sup> In those with BED a greater percentage of energy was consumed as fat (38.9% vs 33.5%) and a lesser percentage as protein (11.4% vs 15.4%).<sup>136</sup> When the binge eating of forty-eight individuals with BED were analyzed from fourteen day food diaries, typically several types of food were consumed during an episode. The most common items consumed were breads/pasta (64.6%), sweets (cakes, cookies, ice-cream; 56.2%), high-fat meat items (hamburger, fried meat; 45.3%), salty snacks (French fries; crisps (chips), popcorn; 39.6%) and chocolate (18.8%).<sup>137</sup>

Thus a wide range of foods are consumed while bingeing. The prediction that it is invariably or predominantly sweet foods that are consumed during a binge has little support; rather a range of highly palatable foods are eaten.

### 5.4. Opioid antagonists

The examination of the influence of opioid antagonists in well controlled double-blind studies is perhaps the best test that we have of the addiction hypothesis. These data are relevant as a strong argument that rats bingeing on sucrose may become physically addicted was the finding that withdrawal effects, similar to those that result with opioid dependence, resulted following the administration of an opioid antagonist. Withdrawal symptoms were induced by naloxone: "The rats were given a drug to block their opiate-receptors and showed withdrawal signs typical of drug-addicted rats- teeth chattering, paw tremors, and head shakes".<sup>1</sup>

### 5.5. The impact of antagonists in the normal population

As opioid antagonists can be expected to have a different influence depending on whether you are or are not addicted to sucrose, initially their effect in those who are not addicted needs to be established. A review concluded that there is unlikely to be a single opioid mechanism although they play a role in the hedonic response to food.<sup>138</sup> There are several reports that in humans opioid antagonists decrease the pleasantness of sweetened solutions<sup>139,140</sup>

and other meals.<sup>141,142</sup> For example Drewnowski<sup>143</sup> administered naloxone while subjects tasted sugar/fat mixtures. Taste preferences were less when the drug was administered, leading to the conclusion that endogenous opioid peptides may be involved in mediating the preference for palatable foods, particularly those high in fat and sugar.

### 5.6. Opioid antagonists and eating disorders

Initially ideas concerning eating disorders were based on the accepted influence of opiates in those without eating disorders. The consumption of palatable foods release endorphins; opiates stimulate food consumption; opioid antagonists decrease the intake of palatable food.<sup>138</sup> Such information led to the study of the influence of opioid antagonists on food intake in those with eating disorders, with the prediction that these drugs should decrease the intake of palatable foods in those who binge.<sup>144,145</sup> Such a prediction does not imply addiction but rather that there is a food-induced release of endorphins in a similar manner to those without eating disorders.

In contrast the auto-addiction model of anorexia and bulimic nervosa proposed that both these eating disorders are mediated by opiates.<sup>146,147</sup> Dieting was said to release endogenous opiates resulting in three possible responses: an emotional high, a drive to eat and finally to conserve energy physiological adaptations that down regulate metabolism. In those with eating disorders this sequence was proposed to become disconnected with individuals being 'addicted' to a particular stage; for example those with anorexia were said to be addicted to dieting and bulimics to eating. Such a theory is unsatisfactory in that it is unclear why the same mechanism should have a different outcome in different individuals. The theory also has a post hoc quality in that it is only after the eating disorder has been characterized that the mechanism is proposed.

With human addictions naloxone is known to have similar effects to those that result with sugar addicted rats. In the hour after naloxone administration those who were addicted to nicotine showed withdrawal symptoms and reported cravings.<sup>148</sup> Naltrexone and naloxone are competitive antagonists at  $\mu$ - and  $\kappa$ -opioid receptors, and to a lesser extent at  $\delta$ -opioid sites, and are sometimes used for the rapid detoxification of opioid dependence; a procedure that may take place under general anaesthesia to attenuate the rapid and sometimes severe withdrawal symptoms. Naltrexone can be also used to discourage relapse as it prevents opioid mediated pleasure, although you need to be completely opiate free as if they are still in the body instant withdrawal symptoms are induced.

Given the consistent finding that opioid antagonists generate withdrawal in those who are addicted, it is an obvious hypothesis that if 'sugar addiction' occurs then opioid antagonists should induce withdrawal symptoms. If the rat model is a homology, a similar reaction to opioid antagonists would be predicted in humans with BED.

Therefore a number of predictions were tested by examining the reaction of binge eaters to opioid antagonists. The examination of the PubMed database, using the terms naloxone, naltrexone, bulimic and binge produced the studies that are summarized in Table 2. Various hypotheses were examined.

*5.6.1. If binge eaters are addicted to sugar then administration of an opioid antagonist would immediately induce withdrawal symptoms. Such responses would only be observed in those with a history of bingeing*

This prediction contrasts with the response to these drugs in those who are not addicted: "At usual therapeutic doses the

**Table 2**  
The influence of opioid antagonists on those with a history of bingeing.

Study	Design	Subjects	Drug	Side effects	Short-term	Long-term	Comments
Jonas and Gold <sup>149</sup>	Open	Bulimic N = 8	Naltrexone Up to 300 mg/d for 6 weeks	No side effects		Reduction in days bingeing and its duration	Subjects selected because they failed to respond to anti-depressants
Jonas and Gold <sup>150</sup>	Open	Bulimic N = 8 N = 8	Naltrexone 50–100 mg/d or 200–300 mg/d for 6 weeks	5/16 reported nausea		No effect on bingeing with lower dose Fewer days bingeing with higher dose	Subjects selected because they failed to respond to anti-depressants
Mitchell et al. <sup>151</sup>	DB crossover	Bulimic N = 5	Naloxone 6 mg bolus then 0.1 mg/kg/h for 2 h or saline	No side effects. Ratings of anxiety, depression and tiredness did not change.	Decrease in total energy intake		Patients had been actively bingeing for at least 3 months and were encouraged to continue during study
Mitchell et al. <sup>144</sup>	DB crossover	Bulimic N = 16	Naltrexone 50 mg/d or placebo for 3 weeks	Drug well tolerated and nobody withdrew because of side effects		No change in the frequency of bingeing or time spent eating	Dose chosen because it is effective in blocking action of exogenous opiates.
Soll et al. <sup>152</sup>	DB crossover	Bulimic N = 16	Naltrexone 50 mg/k or placebo for 3 weeks			No effect on energy and macronutrient content of diet	Same sample as Mitchell et al. <sup>144</sup>
Alger et al. <sup>153</sup>	DB between subjects	33 obese bingers and 22 bulimic	Naltrexone 100–150 mg/d or placebo for 6 weeks	4 experienced agitation, palpitations and sweating when taking naltrexone		Reduced binge duration in bulimics. Reduced binge frequency in obese bingers	History of alcohol abuse in a proportion of subjects and their families
Drewnowski et al. <sup>145</sup>	DB crossover	20 binge eaters 25 with no eating disorder	Naloxone 6 mg bolus then 0.1 mg/kg/h for 2.5 h or saline	None reported	Decreased hedonic response in all. Decreased intake of sweet/fatty foods in binge eaters		
Marrazzi et al. <sup>146</sup>	Case study DB crossover	Bulimic N = 1	Naltrexone 100 mg/d and saline for 6 weeks. 200 mg/d unblinded	No side effects		Reduced bingeing	Seven year history of binge eating without purging
Marrazzi et al. <sup>147</sup>	DB crossover	Bulimic N = 13 Anorexic N = 6	Naltrexone 100 mg/d and saline for 6 weeks. 200 mg/d unblinded	No symptoms increased by naltrexone		Reduced binge-purging in 18/19 patients	Tested hypothesis that both bulimia and anorexia nervosa are opioid mediated
Maremmani et al. <sup>154</sup>	Open	Bulimia N = 4	Naltrexone 100 mg/d 1 week	None reported		No effect on symptom checklist that included bingeing	A combination of naltrexone and fluoxetine produced complete remission
Maremmani et al. <sup>155</sup>	Case study	Bulimic N = 1	Naltrexone 100 mg/d Response within hour	Marked anxiety/panic attack within hours; cured by withdrawal of drug			History of anxiety. Subject was in a trial but not stated how many did not respond in this way

DB double-blind.

adverse effects of naltrexone are usually transient and mild”, similarly “Adverse effects tend not to be a problem with naloxone”.<sup>156</sup> The most common side effect is nausea but anxiety can occur amongst other symptoms. Given the recent development of the addiction hypothesis no study to date has set out to specifically consider the incidence of withdrawal symptoms but it is normal to report any adverse reactions and these are summarized in Table 2. The majority of those with a history of bingeing did not respond adversely to an opioid antagonist suggesting that they were not addicted. The well tolerated reaction to these drugs was similar to the normal population. A minority of those who binge did, however, respond negatively. Alger<sup>153</sup> reported that two subjects responded adversely to naltrexone to the extent that they speculated that they might have been a higher than normal level of serum opiates, although they found that the response to naltrexone was not predicted by the serum levels of  $\beta$ -endorphin. Similarly Maremmani<sup>155</sup> reported that one subject in a trial of those with bulimina nervosa displayed anxiety when naltrexone was administered: however, the majority of subjects did not respond in this way. As adverse reactions can occur in a minority of those who do not binge it is unclear whether these reports are anything other than a coincidence. There is a need for large scale studies of those who do and do not binge: blood endorphin levels need to be monitored and related to the acute reaction to opioid antagonists. To date we cannot logically exclude the possibility that there is a small minority of those who binge who respond adversely to opioid antagonists by displaying withdrawal symptoms, although the evidence is weak.

In summary the prediction that in binge eaters opioid antagonists will generate withdrawal symptoms is not supported by the experimental evidence.

*5.6.2. The addiction hypothesis suggests that bingeing is an attempt to induce the release of endorphins to counter the adverse effects of withdrawal. It follows that as opioid antagonists further reduce endogenous opioid activity they should in the short-term further induce bingeing, in an attempt to stimulate endorphin release to reverse the effects of withdrawal*

The majority of studies in Table 2 looked at the frequency and duration of bingeing and found that drug administration either was without effect, or alternatively decreased bingeing. The increase in bingeing predicted by the addiction hypothesis was never reported. It might be argued that as several studies lasted for a number of weeks the stage had passed when an initial adverse reaction might be expected. It should, however, be recalled that these longer-term studies considered patients who continued to binge, albeit on occasions to a lesser extent. As such, the patients in these studies were not at a stage of withdrawal analogous to that when naltrexone has been used to prevent relapse with opiate addiction, where the body needs to be completely cleared of exogenous opioids.

*5.6.3. The response to opioid antagonists should occur with a dose capable of blocking opioid activity*

When naltrexone is used to prevent relapse with alcoholism or opiate addiction, a dose of 50 mg or sometimes 25 mg/day is used, a level sufficient to block opioid activity. The studies that reported a decrease in bingeing have used doses above these levels. For example one study found that whereas 50–100 mg/day of naltrexone was without effect 200–300 mg/day decreased bingeing<sup>149</sup>. These data question whether an opioid mechanism is involved, as a dose of naltrexone greater than required to block opiate activity was needed to reduce the frequency of bingeing. It appears that other mechanisms, at least in part, are involved.

*5.6.4. The report that naloxone induces withdrawal symptoms in rats addicted to sugar<sup>1</sup> but not fat<sup>7</sup> leads to the prediction that if ‘sugar addiction’ is the mechanism that underlies bingeing, in those who binge opioid antagonists should selectively influence the choice of sugar rather than fat*

Drewnowski<sup>145</sup> examined the hypothesis that the influence of opiate antagonists would be greater amongst those who displayed bingeing. Snack foods were presented and divided into four categories depending on whether they contained high or low levels of sugar or fat. The high-sugar/high-fat category contained chocolate bars and chocolate containing cookies and candies. The infusion of naloxone, rather than saline, significantly reduced the total energy intake of binge eaters. The reduction in intake was most marked for the high-sugar/high-fat foods, those containing chocolate. The obvious explanation is the response to eating highly palatable foods is partially mediated via opioid mechanisms. Thus drugs such as naloxone reduce the pleasantness of palatable high-sucrose/high-fat foods: a phenomenon demonstrated throughout the population<sup>37</sup> irrespective of whether there is a history of bingeing. Even in rats it is palatability rather than sweetness that is important. Naleid<sup>157</sup> found that when rats were given a choice between a high-fat and a high-sucrose diet, naltrexone only inhibited the intake of the preferred diet, more often fat than sucrose.

In conclusion a consideration of the influence of opioid antagonists offers a valuable test of the possibility of sugar addiction although the hypothesis gains no support from these studies.

## 6. Discussion

A series of predictions developed from the hypothesis that an addiction to sucrose consumption can develop have been discussed. If sugar addiction has played a major role in the increase in obesity, fasting should increase food cravings predominantly for sweet items; cravings should occur after an overnight fast; withdrawal symptoms should prevent a decline in the preference for sucrose; the obese should prefer sucrose containing rather than other palatable foods or find sweetness particularly attractive; sucrose containing rather than other food items should predispose to obesity. These predictions have in common that on no occasion was the behaviour predicted by the addiction model supported by human studies. These findings give no support to much of the popular literature that proposes a widespread addiction to sugar.

Although both the animal literature<sup>147</sup> and the present consideration of human data agree that sucrose, when consumed as part of a normal diet, does not produce physical dependence, the animal literature has led to a more specifically hypothesis. The suggestion is that it is the way that sucrose is consumed that may have a specific role in generating BED.<sup>1</sup> A summary of a symposium that considered food addiction concluded that “...even highly palatable food is not addictive in and of itself. Rather, it is the manner in which the food is presented (i.e. intermittently) and consumed (i.e. repeated, intermittent “gorging”) that appears to entrain the addiction-like process”.<sup>158</sup> The present review therefore also examined various predictions derived from the hypothesis that an addiction to sugar is central to bingeing disorders. Dieting should predate the development of BED as it is only when dieting predated sucrose consumption did rats display ‘addictive type’ behaviour; sweet items should be preferentially consumed while bingeing; dietary style rather than psychological, social and economic factors should predispose to binge-eating disorders; opioid antagonists should cause withdrawal symptoms; BED should develop at a younger age when there is a greater preference for sweetness. Again these various predictions have in common that on no occasion were they supported by human data.

The development of an animal model of eating disorders inevitably offers an implicit model of the cause of such phenomena: it is implied that eating disorders reflect the nature of the diet and eating style. There is, however, a second commonly discussed model: an eating disorder is a response to a pre-existing problem of a psychological or social nature, it is an attempt at a solution albeit not a successful approach. There are wide ranging theories about the aetiology of eating disorders emphasizing biological, psychological, social and family factors. Striegel-Moore<sup>159</sup> argued that this heterogeneity of variables suggests that unidimensional models of aetiology are unlikely to be valid. When Polivy and Herman<sup>160</sup> reviewed the causes of eating disorders they considered socio-cultural factors such as media and peer influences; family factors such as enmeshment and criticism; negative affect; low self-esteem; body dissatisfaction. Although they also considered cognitive and biological factors it is clear that it is rarely suggested that the pre-existing diet is the causal factor. Even if nutritional mechanisms can in the future be shown to play a role in eating disorders, at the most they will only be a partial answer as psychological, social and economic factors are clearly necessary to explain much of the increase in obesity and eating disorders. Most experts will find implausible any suggestion that there is a single mechanism that plays a large role, and although we do not fully understand the details, one thing that is certain is the complexity. Any suggestion that problem eating to a large extent reflects a single causal factor is bound to be wrong. Although the scientists who work on animal models tend to be cautious when drawing conclusions, many in the general population have falsely attributed addictive properties to sucrose, even when consumed in a normal manner.

The purpose of this review was not to suggest that the widespread and cheap provision of palatable foods has not played a role in the increasing incidence of obesity. Rather it is important that the underlying mechanisms are understood so that this knowledge can generate appropriate responses. If addiction to sucrose plays an important role in the development of obesity then various conclusions will follow. If it is falsely believed that sucrose is addictive then inappropriate responses will be made and helpful behaviour will be avoided. Already some have been worried that dieting might not be the best solution if it generates cravings and withdrawal symptoms.<sup>5</sup> If sucrose is the villain then attempts to deal with obesity should concentrate on this ingredient. If sucrose is not central then inappropriately concentrating on this food item will ensure that more beneficial responses will be ignored. For example it has been frequently proposed that we should concentrate on fat as it plays a major role in determining palatability, has a more limited impact on satiation than other macronutrients, and plays a major role in the energy density of the diet.

A more general conclusion is that the use of rat behaviour as an experimental model of the human condition is fraught with difficulties. Before behavioural scientists extrapolate findings obtained with animals it is essential that they consider analogous human data. Only if there are marked parallels in the response of the two species will the use of animal models be informative.

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