Sugar addiction: the state of the science

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Abstract

Purpose

As obesity rates continue to climb, the notion that overconsumption reflects an underlying 'food addiction' (FA) has become increasingly influential. An increasingly popular theory is that sugar acts as an addictive agent, eliciting neurobiological changes similar to those seen in drug addiction. In this paper, we review the evidence in support of sugar addiction.

Methods

We reviewed the literature on food and sugar addiction and considered the evidence suggesting the addictiveness of highly processed foods, particularly those with high sugar content. We then examined the addictive potential of sugar by contrasting evidence from the animal and human neuroscience literature on drug and sugar addiction.

Results

We find little evidence to support sugar addiction in human
addiction-like behaviours, such as bingeing, occur only in t
behaviours likely arise from intermittent access to sweet ta
effects of sugar.

Conclusion

Given the lack of evidence supporting it, we argue against
scientific literature and public policy recommendations.

Introduction

Between 1980 and 2013, the proportion of overweight (boc
(BMI ≥ 30 kg/m^{-2}) adults rose from 28.8 to 36.9 % worldv
adolescents [1]. The accompanying costs of health consequ
estimated to range from $3.38 to 6.38 billion annually in th
problem [2]. The scale and impact of the obesity pandemic
demands extreme care and careful scrutiny of existing evid
concepts. In this spirit, we wish to evaluate sugar addiction
consequences in terms of public policy and health advice if

The food addiction (FA) model asserts that excessive consu
the same neurobiological framework as drug addiction. The
Diagnostic and Statistical Manual of Mental Disorders (DS
neuroscientific literature. It is characterised by loss of contr
consume, and a persistence of drug taking despite negative
behaviours has been extensively studied (see [3, 4]). Indivi
symptoms analogous to those of drug abuse, including loss
foods' [5]. Theron Randolph first used the term 'food addic
consumption of various foods, such as corn, milk, eggs, an
changed since this original description (see [7]), and there i
in sugar and fat, are most likely to be addictive. FA researc
addiction will open new avenues for prevention, treatment,
other aspects of the model, has been questioned [10, 11].

Sugar addiction represents a specific case of the FA model in which the addictive substance is the specific nutrient sugar. In this perspective article, we consider the state of the evidence in support of sugar addiction in humans and provide a critical review of the preclinical neuroscience research that has identified sugar addiction in rodent models. This is important because few studies have specifically examined sugar addiction in humans, and the bulk of supporting evidence comes from animal work. However, there is a methodological challenge in translating this work because humans rarely consume sugar in isolation. In order to assess the existing evidence, we must first consider whether sugar could be an addictive agent, examining specifically the animal neuroscientific evidence suggested to support this. As the animal neuroscience of sugar addiction draws strong parallels to drug addiction, we review the sugar and drug addiction neuroscience side by side. We go on to consider the human model of FA to determine whether and how it could be applied to sugar.

Characterising (potentially) addictive foods

A general view is that FA is similar to substance addictions, rather than non-substance behavioural addictions outlined in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5, for a different perspective, see [12]), in that certain 'addictive agents' within food produce neurochemical effects in the brain similar to drugs of abuse. The Yale Food Addiction Scale (YFAS [13] and recently the YFAS 2.0 [14]), which is

now the widely accepted measurement tool for studying FA
with respect to 'certain foods'. These scales do not specify
usually consume food with multiple nutrients. Even foods t
nutrient (e.g. sugar-sweetened beverages) have flavour(s) a
the addictive potential of different foods may provide an in
critical in determining addictive potential.

Evidence from rodent models supports high-fat [15], high-s
fat and high-sugar [17] foods as candidates for FA. In huma
that highly processed, hyperpalatable foods are the ones tha
surrounding what might constitute an addictive food poses
two studies have examined the addictive potential of variou

Schulte et al. [5] suggest that certain highly processed food
term can be used for food), such as high potency and rapid
report that such processed foods are strongly associated wi
YFAS. Their findings also demonstrate that fat content and
serving) predict ratings of problematic foods, where proces
more problematic. In this study, highly processed foods we
carbohydrates (high GL) that may also contain low levels c
argue that processing of raw foods increases the foods' 'po
agents' (e.g. fat, sugar, salt) into the bloodstream, as indexe
consumption.

Fowler et al. [19] hypothesised that individuals who develo
would be more likely to have had problems with foods that
this, they used foods listed in the YFAS and categorised the
and sugar content. Findings indicated increased likelihood
endorsed high-GI and high-sugar, low-fat (but not high-sug
the authors concluded that these patients might have experi
undiagnosed FA. These findings should be interpreted in th
retrospective recall of 'problem foods', only two foods (ca
fat. Furthermore, analyses of the relationship between prob
for current or previous psychiatric morbidity, success of su
suggest caution in arguing that such foods are addictive bas
[20].

To describe the difference between foods such as cupcakes and bananas primarily as being one of the degrees of processing is perhaps a rather narrow view, and a strong case can be made for these foods having other important differences relevant to overconsumption and obesity (e.g. energy density). Even leaving this aside, there are several important concerns about both of these studies. First, the potentially addictive foods have been taken from the 'problem foods' list of the YFAS. The scale quantifies FA symptoms with respect to these problem foods, based on the assumption that they are likely to be addictive. Both of the aforementioned studies rely on this assumption and take the evidence that individuals have reported FA symptoms with respect to these foods on the YFAS in several studies, as further supporting the assumption. Second, these findings rely entirely upon participants' perceptions of difficulties surrounding the foods items, which are then linked (by way of mechanistic explanation not empirical evidence) via GL or GI to postprandial glucose and insulin. That is, no direct evidence indicates that these foods are problematic for these individuals because they lead to higher postprandial glucose. Although individual postprandial glucose response (PPGR) has low intra-personal variability, there can be high interpersonal variability in PPGR following the consumption of identical meals [21, 22]. For example, Zeevi et al. [21] found that PPGRs for cookies and bananas varied significantly across participants, suggesting that some individuals may be high glucose responders to 'good' foods and low responders to 'bad' foods. It is also important to note that there are several high-GI foods such as breakfast cereals and baked potatoes that are not included in the list of YFAS problem foods. This suggests that the

potential explanatory power of high GI as a determinant of
looked beyond the list of problem foods. Given the host of
affect glucose regulation, it is important to consider the phy
between the nutrient content of the food and the individual

Third, and most importantly, the proposed model of why hi
lacks a mechanistic link between higher postprandial levels
draw upon a seemingly superficial similarity between the a
speed of absorption, to explain why processed foods are lik
between the processing of grapes to wine, poppies to opiun
transition from naturally occurring substances/food to drug
this formulation of highly processed foods only captures th
overlooking the critical pharmacodynamic effects. The coc
which can be enhanced by increasing the dose of the active
foods, studies show that moderate increases in blood gluco
cognitive performance in a variety of tasks, including sema
and even driving performance [25]. Few functional MRI st
brain function as it relates specifically to hedonic eating bel
fasting nor postprandial blood glucose affected the blood-o
cues in several brain regions (e.g. amygdala, pallidum, insu
men, increased postprandial blood glucose levels have beer
in regions associated with reward processing [27]. Given th
glucose supply to the brain, it is perhaps not unexpected tha
effects on brain function. In short, the notion of increased d
increased addictive potential is questionable when it comes

Is sugar a potentially addictive substance?

The FA literature considers sugar (and other refined carboh
high addictive potential, contributing to their GL (dose) and
discussion of sugar has centred on its palatability or hedoni
has both hedonic and caloric value, and these two aspects b
of its consumption, respectively. Moreover, these aspects a
processing as demonstrated in two elegant sets of experime
concentrating hormone (MCH)-expressing neurons located within the lateral hypothalamus respond to
extracellular glucose levels and project to dopaminergic (DA) neurons in the striatum and midbrain regions. The
animals show a preference for sucrose over the non-nutritive sweetener, sucralose, and the glucose-sensing
ability of these neurons is critical in determining this, as transgenic mice lacking MCH neurons do not show this
preference [28]. MCH neurons encode the rewarding nutrient properties of sucrose by increasing striatal DA
release independently of gustatory input. Optogenetic stimulation of MCH neurons during consumption of
sucralose leads to striatal DA efflux and preference for sucralose over sucrose [28].

Recently, Tellez et al. [29] expanded upon this work by examining DA transmission in the striatum in response
to oral sucralose intake versus intra-gastric glucose or sucralose administration. Using microdialysis, the authors
reported changes in DA release in the ventral and dorsal striatum, where regional DA release selectively encoded
the pleasurable and nutritional value of the sweet foods. Sucralose consumption was linked to enhanced DA
efflux in the ventral striatum (VS), which was no longer observed following devaluation of the sweetener with a
bitter additive. Conversely, intra-gastric infusion of glucose, but not sucralose, elicited DA release in the dorsal
striatum (DS). Thus, the VS and DS appear to encapsulate functionally distinct responses to palatable and
nutritive signalling, and the authors went on to delineate the role of D1 and D2 striatal DA neurons in
palatability and nutrient preferences. Dopaminergic signalling excites D1 DA neurons while inhibiting their D2
DA counterparts, and this interaction modulates the control of goal-directed actions, including overeating [17].
Optogenetic stimulation of D1 DA neurons within the DS and substantia nigra terminals increases consumption
of a bitter sucrose solution, which supports the dorsal basal ganglia pathway as a circuit that is selectively

responsive to the nutrient properties of sugar reward [29]. I
D1 DA, and D2 DA neurons has yet to be explored in anim
aforementioned neural circuits reflect processes underlying

This experimental work allows us to consider that addictive
mechanisms: one related to palatability and the reinforcing
and post-ingestive effects, and a third arising from a combi
'addictive' quality of sugar may be restricted to its sweetne
Of course, only the third possibility would support sugar as
where highly processed foods with added sugar would be v
therefore potentially have a characteristic profile of ingestiv
often consume sugar in combination with other nutrients, d
and low addictive potential would need to be characterised
foods can have very different post-ingestive profiles in diff
aspect of individual vulnerability to a potentially addictive
little work in humans has examined them directly. The anir
evidence of parallels between sugar and drugs. We conside
overview of the neurobiological characteristics of drug add

Animal models of drug addiction

Prevailing models of drug addiction emphasise changes in
mechanisms involved in the transition from voluntary drug
releases DA within the mesolimbic system which reinforce
of, and subsequent motivation towards, drug-related cues [
accumbens (NAcc) shell, yet this response becomes blunte
[31]. Instead, drug-related cues produce an anticipatory DA
[32]. This has been framed as an increased anticipatory rew
Activation in the dorsal striatum and basolateral amygdala
becomes increasingly elicited by drug-related cues, it is ult
habit [33]. This transition from goal-directed to habitual dr
rodent models of addiction to cocaine, heroin, and alcohol
humans. These compulsive behaviours arise from functiona
salience, compulsivity), as well as the dorsolateral and infe

The onset of drug addiction has been associated with decreased availability of DA D2 receptors in both humans and non-human primates [36, 37]. These findings relate low DA receptor availability to increased trait vulnerability to drug abuse; however, it has been argued that chronic drug use reduces the number of DA D2 receptors, thus resulting in a 'hypodopaminergic' system [38]. While it is likely that aberrant DA D2 receptor numbers reflect both cause (trait vulnerability to) and consequence of prolonged drug use, reduced DA D2 receptor availability has been closely tied to withdrawal symptoms and the development of drug tolerance, in which drug consumption no longer elicits a positive effect but rather mitigates a negative state [39, 40]. Together with afferent input from the amygdala, these neuronal changes in the striatum (i.e. reduced DA D2 receptors) perpetuate drug use to avoid dysphoria and withdrawal, comprising what Koob and Le Moal [41] have termed the 'dark side' of addiction.

Accordingly, in sugar addiction, one could expect to see a similar behavioural and neurobiological syndrome. Voluntary consumption of sugar under goal-directed control would increase DA release in the mesolimbic system, enhancing the salience of and motivation for sugar. Over time, sugar seeking and consumption would become habitual and compulsive with an accompanying shift from ventral to dorsal striatal control, as well as changes in prefrontal cortical control of these behaviours. These neural adaptations would serve to perpetuate sugar seeking that may also be driven by the need to avoid withdrawal symptoms. In line with research of chronic drug use, DA D2 receptor levels may represent a vulnerability marker and also result as a consequence of excessive sugar intake over time, regardless of BMI status or obesity.

Comparison of drug addiction and su

Critical to these studies are the experimental designs used t
believe that a working knowledge of these paradigms and t
literature on animal models of drug and sugar addiction. Th
paradigms, and we will compare different aspects of drug a
have been drawn between sugar and a variety of illicit drug
have chosen to focus on the neurobiological effects of coca
system, and heroin, an opiate that acts upon both dopamine
point out at the outset that sugar addiction literature is not a
therefore, not all aspects of addiction have been examined

General overview of experimental models

Drugs

Rodent models of addiction traditionally frame the drug of
associated with a pleasurable outcome. A drug is thought to
response to the agent exceeds the response to a control, e.g
administer the drug for a short daily session of 1 to 3 h [42
trained to self-administer intravenous (IV) cocaine via a lev
where each lever press prompts drug delivery (a fixed ratio
or intravenously, though it is often preferred to use the rout
into consideration taste effects. Thus, implanted catheters a
but some studies allow access to an oral cocaine–sucrose so
protocols train rodents to self-administer drugs of abuse pri
vulnerability to drug addiction. As such, the use of drug-na

To model the transition to compulsive 'drug seeking', the r
which they must systematically work harder (i.e. increase t
Motivation is further measured by 'breakpoints', or the rati
the reward, and it can be augmented by periods of drug abs
will work for the drug despite negative consequences—a k
stimuli (e.g. lever press) or outcomes are paired with aversive outcomes, such as an electric footshock or
nauseating chemical additive. Following extensive drug self-administration, rodents display withdrawal
symptoms in response to forced abstinence, as well as dopamine (e.g. sulpiride) and opioid (e.g. naloxone)
antagonists. However, drug seeking can be extinguished throughout periods of forced deprivation by replacing
the cocaine or heroin infusion with saline (for a complete review, see [46]).

In human addiction, habitual drug-seeking and drug-taking behaviour, even following sustained abstinence, is
often elicited by environmental cues, acute stress, or drug exposure. Second-order reinforcement schedules
represent one method by which cue-elicited reinstatement of drug seeking can be studied in animals [47]. The
drug infusion is paired with an additional conditioned stimulus (e.g. illuminated light, tone) following which
exposure to the conditioned stimulus has been shown to reinstate cocaine-seeking behaviour [48] and morphine
administration [49] following abstinence. More recently, the conditioned place preference (CPP) paradigm has
become a widely used design, in which rodents associate distinct environments with drug and saline infusions.
Following abstinence, re-exposure to these environments, along with drug priming, leads to the reinstatement of
habitual cocaine and heroin-seeking behaviour [50], thus modelling the circumstances under which humans often
experience drug relapse.

Sugar

Although sugar (e.g. sucrose, saccharin, glucose) reinforce within drug addiction studies, Avena et al. [16] have demo develop addiction-like behaviours with respect to sugar. Af et al. [51] claim to, '[…] still use the same basic technique a feeding schedule that repeatedly induces sugar bingeing a deprives rodents of food for 12 h (or in some instances, 16 subsequent 12 h, during which the rats may consume either 25 % glucose solution or a 10 % sucrose solution; the latte the 12-h period of food availability begins 4 h into the dark the likelihood of consuming a novel food [51]. An importa experiments is that unlike the drug models, which increasi usually had previous access to sucrose and are selected for possibility of these animals having a vulnerability to develo this schedule for 3 to 4 weeks begin to develop signs of ad additional review). It is important to emphasise these addic intermittent access regimes and not with ad libitum access.

Bingeing

Drugs

Following initial self-administration training, increased acc associated with enhanced, binge-like consumption [55–57] infusion develop a binge-like pattern of consumption that i highly variable after 24 h, where increased time between bi [58]. Interestingly, binge-like self-administration of heroin rodents self-administer the most heroin at the start of the se stable level throughout the session [57]. The reinforcing ef and moderate doses have been shown to elicit reinforcing e

Acute IV administration of cocaine preferentially increases to the NAcc core [60], and this is associated with the acute DA release in both the ventral tegmental area (VTA) and th of mu-opioid receptors (MOR), which triggers a neurochem release [61, 62]. Mesolimbic DA release elicits hyperactivity and euphoric effects following cocaine and heroin infusion, respectively. These effects can be inhibited (as evidenced by reduced self-administration) by lesions to the ventral pallidum, as well as D1 receptor blockade in the central nucleus of the amygdala, in cocaine-conditioned animals [63, 64]. As heroin has high affinity for MOR and delta opioid receptors (DOR), administration of selective MOR and DA agonists has been shown to result in heroin reinforcement that is extinguished following chemical lesioning of DA neurons or microinjections of opioid receptor antagonists within the VTA [65].

Sugar

Binge-like sugar consumption has been observed in rodents under both 24-h and intermittent reinforcement schedules, where animals self-administer sugar on an FR1 protocol. Colantuoni et al. [66] reported that food-deprived rats increased sugar intake within the first hour of access to food, and similar bingeing patterns occur when rats receive 12-h access to both sugar and chow [51]. With the same intermittent reinforcement schedule, sham-fed rodents consume more sucrose than real-feeding controls [67], although differences are non-significant with repeated consumption. Interestingly, rodents with ad libitum access to sugar solution consume the food throughout the light phase (or inactive cycle), and total sugar intake does not differ between rodents with 12- versus 24-h access [16]. Moreover, rats fed daily intermittent sugar and chow offset sugar consumption by decreasing chow consumption, thus regulating caloric intake and preventing weight gain [68, 69]. Because

rodents with ad libitum sugar access offset caloric intake ar
al. [16] concluded that such experimental conditions canno
intermittent access is critical to the development of binging
to develop addictive behaviours. With respect to obesity, it
and ad libitum access schedules offset chow intake to comp
stability.

These behavioural data highlight noteworthy differences be
apparent distinction arises from temporal discrepancies rela
abuse. Despite limited evidence of food restriction increasi
increase *both* cocaine and heroin intake under normal feedi
85 % body weight (e.g. [71]). Under such conditions, it is p
abuse versus non-drug rewards; however, these processes b
following food restriction. As similar findings are seen in s
from the reinforcing effects of a preferred flavour, rather th
libitum conditions, rats dramatically increase cocaine intak
rats continue to binge throughout the 72-h period [58]. Min
to bingeing patterns that converge with an inherent circadia
administer cocaine during the light phase [72]. Yet, binge-l
consummatory pattern with binges occurring early in the fo
homoeostatic regulation of feeding behaviour and the prese

The neurobiology of sucrose reinforcement has largely focu
core. Intermittent sucrose consumption persistently increas
response to sugar in both sham [67] and normal feeding [16
control or ad libitum sugar access animals, and as with mos
[73, 74]. Thus, a drug-like DA response to sugar is only ob
suggesting a critical role of the paradigm. Corwin has raise
of eating under uncertainty because food availability is unp

Infusion of a selective mu-opioid agonist into the NAcc has
chocolate) with identical nutrient profiles, suggesting that i
flavour rather than sucrose preference [77]. Additionally, M
intake [78]. Infusion of naltrexone (an opioid antagonist wi
decreased consumption of the preferred flavour, yet system
equally. These findings, along with those of Tellez et al., demonstrate distinct neural mechanisms for sweetness and caloric content, and support the role of rewarding effects of sweet taste in this intermittent access paradigm. Benton [54] and Dileone et al. [79] have previously argued the post-ingestive properties of glucose appear to have little effect on initial consolidation of its rewarding properties. Moreover, neurobiological changes in the striatum have yet to be reported in the absence of the intermittent sugar binging (i.e. with ad libitum access to sugar) [66]. In summary, the dopaminergic changes that resemble addiction only occur with sugar consumption under the intermittent access regime, and without these conditions, the dopaminergic response to sugar resembles that to other natural rewards. Conversely, cocaine and opiate drugs cause neurobiological changes within the NAcc and VS that lead to and perpetuate addiction, including changes in D2 DA receptor levels [3] and MOR density and expression [80] following chronic cocaine and opiate administration, respectively.

Motivation and substance seeking

Drugs

Following initial self-administration training, rodents show increased motivation for cocaine self-administration as evidenced by high breakpoints within PR schedules. Breakpoints may be manipulated by several experimental parameters, including the unit injection dose and restricted access to cocaine. For example, rats that were allowed access to cocaine 4 times/h in a 24-h period during initial self-administration showed higher breakpoints

after 7 days of abstinence when compared to rats that were
assert that a progressive increase in daily breakpoints is not
speed of the injection. For example, in rodents with a histo
doses had significantly higher breakpoints than those that r
testing, speed of initial cocaine infusion significantly altere
rodents receiving cocaine infusions over 5 s versus those re

Unlike cocaine seeking, the emergence of heroin-seeking b
withdrawal symptoms, which result in increased consumpti
of a dysphoric state). Acute opiate exposure increases pain
sensitisation of nociceptive systems may be related to the d
reinforcement [57, 84]. Both forced deprivation and opioid
characterised by teeth chattering, paw tremors, and erratic a

Cocaine abstinence increases motivation in rodents initially
the establishment of cocaine as a positive reinforcer power
Moreover, Vanderschuren and Everitt [71] demonstrated th
suppress cocaine seeking in rodents with a prolonged cocai
authors assessed drug-seeking behaviour within a heteroge
seeking and taking cocaine are distinct acts with separate le
lemon–sucrose solutions with an aversive lithium chloride
sucrose solution as rodents maintained the same level of dr

Changes in the limbic, cortical, and ventral striatal circuitry
[34]. Lesioning of either dopaminergic circuitry in the basc
NAcc core alters cocaine seeking [86]. In contrast, lesionin
[87], likely by way of diminished executive control, as this
(pDMS) and reciprocally to the basolateral amygdala [34].
development of enhanced motivation for morphine. Mice la
saline infusions on FR or PR schedules [88]; however, rode
the NAcc and DS demonstrate significantly higher breakpo
[89]. Thus, converging neurobiological evidence identifies
maintenance of opiate seeking. Over time, these neurobiolo
seeking and intake, resulting in the hallmark feature of add

Sugar

Enhanced motivation and sugar seeking are often achieved by forced deprivation, which has increased the number of lever presses for self-administration of sucrose solution [16]. However, these findings do not directly represent rodents' motivation for a sugar reward but rather the number of unsuccessful lever presses executed under an FR1 schedule (i.e. the lever presses in between sugar receipt). Receipt of sugar reward was not dependent upon the number of additional presses between reinforcement. A more recent study has incorporated differential reinforcement schedules, which systematically increase the time intervals between sucrose reinforcements to quantify impulsive responding for sucrose solutions [90]; however, the findings failed to demonstrate increased lever pressing across sucrose-reinforced sessions as compared to control (i.e. water) sessions. As such, motivation for sucrose appears to be less robust than that for either cocaine or heroin, though expectedly infusion of a selective mu-opioid agonist significantly increases break points for sugar pellets in a progressive ratio schedule [91].

Some research has quantified motivation for sucrose by direct comparison with other drug-seeking behaviours. In one study, some rodents preferred self-administration of saccharin over cocaine and paid a greater 'price' for saccharin than for cocaine by adhering to FR2, FR4, and FR8 reinforcement schedules [53]. Although this resembles early PR schedules in which rodents linearly increased lever presses for subsequent infusions, standard PR schedules for drug reinforcement now require rats to increase lever presses exponentially from one

infusion to the next [55]. Thus, direct comparison of these
heroin reinforcement overestimates the degree to which sac
saccharin selectivity increased cocaine consumption follow
effect(s) of sweet preference on vulnerability to drug addic
preference for Oreo cookies has predicted greater break po
rodents that preferred rice cakes demonstrated equivalent s
cocaine-seeking behaviour [93].

Habitual use and withdrawal

Drugs

Rodents with extended cocaine self-administration training
cocaine was administered, even following periods of abstin
stimulus (i.e. a light previously paired with lever pressing)
behaviour [48] and morphine administration [49] following
injections following abstinence, and the CPP paradigm rest
behaviour, thus modelling the circumstances under which h

Whereas the acute reinforcing effects of cocaine are associa
NAcc shell, cocaine seeking has been related to enhanced I
of DA receptors in the anterior dorsolateral striatum, but nc
Jedynak et al. [98] further demonstrated that prolonged stir
by increasing dendritic spine density in the dorsolateral sub
dorsomedial subregion. The authors assert that such restruc
the emergence of S–R habits following chronic stimulant u
behaviours. As discussed above, in the case of heroin, the c
drug use as negatively reinforced by the dysphoria of withc

Sugar

Although compulsive sugar-seeking behaviour following e
converging evidence suggests that animals develop CPP in
sugar, food-deprived rodents prefer the environments in wh
[100, 101], and similar findings were reported with high-sucrose food rewards [102]. Administration of naltrexone dose-dependently disrupts CPP for sucrose, yet the opioid antagonist does not affect the development of CPP [103]. The competitive opioid antagonist naloxone precipitates withdrawal symptoms in sugar-bingeing rats, which resemble those of opiate withdrawal (e.g. anxiety, teeth chattering, forepaw tremor, head shakes) and share a similar neural profile with decreased DA and increased acetylcholine in NAcc [66]. Furthermore, Avena et al. [104] report increased anxiety in fasted rodents (36 h) that were previously maintained on an extended intermittent reinforcement schedule with 10 % sucrose solution. A similar withdrawal syndrome has been observed following 8 days of an intermittent access to saccharin [51]. It has also been demonstrated that rats on the intermittent access schedule show reduced D2 DA receptor binding in the DS [66].

A shared neurobiology?

An oft-repeated observation asserts that food and drug consumption share a common neurobiology [105]. This is true in so far as drugs are understood to ‘hijack’ a neural system that primarily processes natural rewards like foods; however, important differences remain. First is the matter of the anatomical localisation of the neural circuits involved in these consummatory behaviours. Carelli et al. [106] have demonstrated that different populations of neurons in the NAcc respond to cocaine and natural rewards. Second, the dopaminergic response to sugar (and other foods) rapidly habituates, and it is attenuated by predictive cues such as smells; however, the DA response to cocaine does not habituate and is enhanced by predictive cues [31]. Third, when cue pairing to

the delivery of either sugar or cocaine is established, the cu
case of sucrose, the DA level rapidly returns to baseline an
consumption of sucrose [107] whereas in cocaine, the surg
lever pressing and cocaine delivery [108]. Fourth, Pavlovia
core, whereas those conditioned to drugs of abuse release D

Summary of the animal neuroscience

Clearly, addiction-like behaviours can be elicited by sucros
First, as evidenced by the studies using sucrose in sham-fe
saccharin, it seems that these behaviours occur in response
content. Both of these findings raise another important que
sucrose that are important to the development of this addict
effects of drugs are critical to the development of the neuro
behaviours are only engendered in a specific intermittent ac
development, as these behaviours are not seen in animals g
regime, test animals have been pre-selected for sucrose pre
animal models of drug addiction where drug-naïve animals
the prevalence of addictive-like sucrose consumption rema
addiction, where it has been estimated that between 5 and 2
drug addiction [110–112]. Clearly, the combination of swee
strongly resembles addiction in several aspects, including a
[68, 113] that seems to be mediated by mu-opioid receptor

However, even in the intermittent access model, there rema
addiction. To date, increased motivation for sucrose has be
implemented progressive ratio schedules to measure the ro
extended access to sugar remain susceptible to devaluation
agent, whereas cocaine- or heroin-addicted animals continu
The extent of habitual responding to sugar remains underst
sucrose seeking has yet to be characterised. In contrast, the
drug-seeking behaviours in animals with historic cocaine o
seeking in response to environmental cues represents a hall
like consumption of sugar diverges from drug addiction on
suggesting a need for great caution in drawing parallels between sugar and drug addiction.

Sugar addiction in humans

There has been little empirical work examining sugar addiction in humans. Given this, we consider how sugar addiction, as a specific form of FA, might be conceptualised in humans, and we summarise experimental challenges in evaluating it, beginning with a brief overview of FA.

The behavioural phenotype of food addiction: the YFAS and YFAS 2.0

The current FA phenotype was first operationalised in the 25-item Yale Food Addiction Scale (YFAS; [13]). Both the FA model and the YFAS conceptualised FA in terms of a translation of DSM-IV substance dependence [114] to food. Criteria include persistent eating despite negative consequences, persistent desire for food, unsuccessful attempts to cut down and impairment of functioning because of overeating. The criteria are defined with respect to ‘certain foods’, and the YFAS provides 21 examples from 5 food categories: sweets (e.g. ice cream), starches (French fries), salty snacks (pretzels), fatty foods (pizzas), and sugary drinks. The YFAS can provide a ‘diagnosis’ of FA if at least three criteria are endorsed along with clinical impairment, or a ‘symptom count’ to indicate severity of symptomatology (scores range from 0 to 7). It has become a popular and widely

used self-report measure of this construct to the extent that
validity and utility have been questioned [10, 11].

The YFAS has recently been updated [14] based on DSM-5
in the YFAS 2.0. The key difference is that, in updating cri
abuse and dependence, the threshold for diagnosing FA has
clinically significant impairment may be diagnosed with m
severe (6 or more symptoms) FA. Preliminary validation of
meet criteria for FA, and 11.9 % of the sample met the thre
and obese individuals endorsed more FA symptoms than th
severe FA was highest in the obese weight class [14]. Altho
and convergent validity in the YFAS 2.0, previously expres
of withdrawal symptoms and tolerance and how they might
main concern is not that their presence is critical in FA; rat
fact that they are not adequately defined and may therefore
Moreover, withdrawal is frequently endorsed by participan
study of the YFAS 2.0, there seems to be strong concordan
YFAS 2.0 [14]. It is important, therefore, that they are char
precise definition, it is difficult to determine conclusively th
symptoms to a particular nutrient or food. Indeed, if a with
would offer important clues as to the nature and mechanism
it is important to acknowledge the difficulty posed by the la

Does food addiction represent a distinct phenot

FA has several shared features and high levels of co-morbi
which raises the question: could it be that YFAS is indirect
opposed to defining a distinct syndrome? BED is characteri
of food with loss of control over eating, which is often don
disgust. It is associated with weight gain, but a significant p
with BED have been proposed to be the strongest candidate
that FA represents an atypical subtype of BED based on a g
shared genetic vulnerabilities to drug abuse and binge eatin
exhibit poor impulse control and emotion regulation, as we
FA liability [118]. Davis et al. [119] found that BED was associated with the A118 polymorphism of the mu-opioid receptor gene (*OPRM1*) and the Taq1A A1 polymorphism of the dopamine D2 receptor gene (*DRD2*), both risk factors for substance use disorder. This same group also identified a dopaminergic multilocus genetic profile that is uniquely associated with FA when controlling for binge eating behaviours [120]. These data suggest a similarity between FA and substance addictions, but require further exploration in well-powered studies with the appropriate diagnostic groups is necessary.

Long et al. [116] recently carried out the first systematic review of the YFAS literature. They examined 40 published articles to address important outstanding questions about FA, including its relationship with BMI and eating disorder pathology and whether FA represents a distinct phenotype of disordered eating. The authors found a high co-occurrence of FA with BED and bulimia nervosa. An estimated 47.2 to 56.8 % of people with BED meet criteria for a FA 'diagnosis' [116], and these prevalence rates seem excessive for a diagnostic subgroup. Binge eating frequency correlated with YFAS scores in both overweight and healthy weight groups, but the relationship with BMI was less clear-cut. Some studies report non-significant differences in BMI across YFAS-diagnosed 'food addicts' and their healthy counterparts [121], while others indicate no correlation between BMI and YFAS score [122, 123]. While the prevalence rates of FA are consistently greater in overweight and obese groups (15.2 to 56.8 %), whether FA accounts for enough unique variance in obesity to be considered an explanatory mechanism for this condition remains unclear. Furthermore, the highest prevalence rates of FA have been reported in individuals with bulimia nervosa (83.6 %) [124, 125]. This finding should be interpreted cautiously as the numbers of individuals with diagnosed bulimia nervosa in these studies is small.

Nevertheless, as these individuals often maintain a healthy
dissociable from BMI, particularly amongst those who hav
summary, the findings of Long et al. [116] provide evidenc
correlates of FA and suggest poor discriminant validity of t

Defining a sugar addiction in humans

Defining sugar addiction in humans remains challenging. F
supports sugar as an addictive substance, and the animal ne
palatability to be critical elements of addictive-like eating.
the 'substance' of interest. Even so, there remain important
relates to addictive potential and whether sugar is necessary
precise, and given a commonplace behaviour like consump
of consumption that separates normal from disordered intal
criteria for individual items and a necessary overall impairr
preliminary, examination of dietary profiles associated with
consumption of energy-dense, nutrient-poor foods (e.g. can
score and BMI [126]. Interestingly, dietary intake of carboh
FA diagnoses or scores, suggesting a limited role of sugar i
whether FA represents a distinct phenotype remains unclea
is a particular difficulty. Distinguishing individuals with BI
those with a sugar (or sweet food) addiction will be a challe
phenotype.

An alternative approach would be to consider whether aspe
similarity with addiction-like behaviours, such as cravings
reports food cravings, particularly for palatable foods like c
cravings in terms of their intensity, their reported frequency
short-lived and subside with fasting as opposed to drug cra
with abstinence [54, 127]. Rogers and Smit [127] have pro
in terms of ambivalent attitudes to particular foods. Thus, f
but one that should be eaten with restraint. Attempts to rest
preoccupying, and this is experienced as a craving and hen
alternative approach asks whether there is an addictive aspe
highly debatable.

Conclusions

In this perspective article, we have reviewed the current state of the evidence for sugar addiction. Most of the evidence is limited to the animal neuroscience literature, and it is far from convincing. Importantly, several key elements of drug addiction have not been evaluated in sugar addiction models, such as the transition to compulsive drug-taking and dose-dependent effects on addiction liability. There remains a paucity of human evidence in this area, and we did not consider the literature encompassing the behavioural and neural effects of sweet or palatable food consumption as this would be far too indirect to the question of sugar addiction. There is the problem of the dearth of data on pure sugar consumption as we rarely consume sugar in isolation, and the ecological validity of studies examining pure sugar consumption in humans would be limited.

In terms of future directions, we suggest two areas of potential interest. The first is to examine whether sweet foods with high GI/GL might cause a food addiction in humans. We have discussed the significant methodological and conceptual limitations of the human FA model and its measurement instruments, the YFAS and the YFAS 2.0, which will need to be considered in such explorations. The second is to examine the relevance of the intermittent sugar access schedule used in animal models to the development of eating disorders (and perhaps even a form of FA) in humans.

In summary, the science of sugar addiction at present is not very popular and powerful idea, but as this special issue illu comes to misconceptions about sugar. Even the most perfu explanatory power the term 'sugar addiction' has when use in the context of major public debates such as those over th the UK. Although the concept as we discuss it here is far m of whether sugar addiction is a useful (if not valid) concept environment? From a policy perspective, it is unlikely that its presence in numerous food items, and any analogies sug be specious. Given the multitude of interacting factors that we argue that support of sugar addiction as a primary causa narrow view that fails to capture the complexity of these co and appropriate responses. Furthermore, while there is a pr argue that it is dangerous to draw strong conclusions about evidence. There are many strong arguments for cutting dov products accordingly, yet these arguments will all stand or

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Ethical standard

This article does not contain any studies with human participants or animals performed by any of the authors.

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