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The obesity epidemic: Is glycemic index the key to unlocking a hidden addiction?

Simon Thornley [a,*], Hayden McRobbie [b], Helen Eyles [c], Natalie Walker [c], Greg Simmons [a]

[a] *Public Health Medicine Registrar, Auckland Regional Public Health Service, Private Bag 92 605, Symonds Street, Auckland, New Zealand*
[b] *Department of General Practice and Primary Health Care, University of Auckland, Private Bag 92019, Auckland, New Zealand*
[c] *Clinical Trials Research Unit, School of Population Health, University of Auckland, New Zealand*

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''When you are addicted to drugs you put the tiger in the cage to recover; when you are addicted to food you put the tiger in the cage, but take it out three times a day for a walk. (Kerri-Lynn Murphy Kriz [1])''.

Summary High body mass index (BMI) is an important cause of a range of diseases and is estimated to be the seventh leading cause of death globally. In this paper we discuss evidence that food consumption shows similarities to features of other addictive behaviours, such as automaticity and loss of control. Glycemic index is hypothesised to be the element of food that predicts its addictive potential. Although we do not have substantive evidence of a withdrawal syndrome from high glycemic food abstinence, anecdotal reports exist. Empirical scientific and clinical studies support an addictive component of eating behaviour, with similar neurotransmitters and neural pathways triggered by food consumption, as with other drugs of addiction. The public health implications of such a theory are discussed, with reference to tobacco control. Subtle changes in the preparation and manufacturing of commonly consumed food items, reducing glycemic index through regulatory channels, may break such a cycle of addiction and draw large public health benefits.

Introduction

Obesity is globally estimated to be the seventh leading cause of mortality [2]. Despite knowledge of the health consequences, the prevalence of overweight and obesity continues to increase in the western world. Over the last 25 years, the proportion of Americans categorised as obese (BMI $\geqslant$ 30 kg/m^2) has increased from 14.5% to 32.2%, and is projected to rise further [3]. The predominant view of the epidemic, at present, is that this rise in obesity results from an obesigenic environment – with a decline in metabolic output from reduced levels of physical activity and/or an increase in energy intake of food

* Corresponding author. Tel.:+64 212991752; fax: +64 9 630 7431.
E-mail address: sithor@woosh.co.nz (S. Thornley).

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that is cheap and energy dense [4]. Despite a growth in programmes and awareness from this knowledge, little progress toward lowering the prevalence of obesity has been made.

One much studied property of carbohydrate containing food in the last 10–15 years is glycemic index (GI), a measure of how fast and how much a food can raise plasma glucose levels following ingestion. A standardised (50 g) bolus of pure glucose is given a glycemic index score of 100, and the area under the curve (plasma glucose vs. time) of 50 g of carbohydrate in comparator foods can be measured [5]. Although exceptions exist, refined high starch carbohydrates such as white bread are high GI ($\geqslant$70), whereas low starch vegetables, legumes and dairy are low GI ($\leqslant$55). Glycemic load (GL) is the glycemic index multiplied by the mass of carbohydrate. Diets based on low GI foods have proved popular in the lay press, with over 2 million copies of the book ''The New Glucose Revolution'' sold [5].

In the scientific community, the significance of GI has been hotly debated in recent years [6]. A meta analysis published by Barclay et al. showed that low GI/GL diets have a small but protective effect on the risk of chronic diseases such as type 2 diabetes, coronary heart disease, gallbladder disease, breast cancer and all diseases combined (Rate Ratio 1.14, 95% CI 1.04 to 1.15) [7]. The effects on obesity and satiety are not conclusive; however, small studies have shown significantly more weight loss in selected subjects on low GI diets, compared with those on higher GI diets. For example; a cross over study by Slabber et al. of hyperinsulinemic women showed more weight loss after 12 weeks of consuming an energy restricted low compared to high GI diet (−7.4 kg vs. −4.5 kg; $P = 0.04$) [8]. In a more recent study of 40 subjects with type 2 diabetes, randomised to either a low GI or standard diet (in which subjects were counselled to consume 55% of total energy from carbohydrate sources), no significant weight loss change was noted between the groups after 12 months, however, the low GI group were less likely to require increases in diabetic medicines (odds ratio 0.26, $P = 0.01$) [9]. The significance of GI contributing to obesity at both the level of the individual and population is therefore not yet known.

Despite uncertainty over outcomes from low GI/GL diets, the physiology of glucose absorption shows remarkable parallels to that of nicotine from tobacco. In this paper we contrast and compare knowledge of nicotine addiction and the addictive potential of nicotine containing devices to food and GI. The idea that obesity is caused by addictive mechanisms, similar to other drugs is not new, and parallels have been previously drawn, both in the scientific and lay literature [10]. However, GI has not been implicated as the predictor of the addictive potential of foods, and such addiction is commonly attributed to a small subset of the obese population [11,12].

Hypothesis

Addiction to high GI foods is proposed to be an important factor causing the obesity epidemic. Further, GI may be the key mediator of the addictive potential of food. In this paper we explore the nature of addiction, whether the pathophysiology and symptoms of obesity are consistent with addiction, with reference to what is known about the neuroscience of appetite regulation and the patterns of behaviour observed with established addictions. The implications of this theory are linked to the treatment of other drug addictions and actions that have proved effective to reduce harm at a policy and individual level.

Addiction — definition and mechanisms

What is addiction? Uncertainty exists, but *a loss of control* is central, often linked to drug taking behaviour [13]. Physical dependence is a related phenomenon – associated with physiological adaptation to a drug which is taken to prevent withdrawal symptoms. The Diagnostic and Statistical Manual-IV (DSM IV) [14] criteria for substance use are commonly used to adjudicate addiction in the individual. These criteria, summarised, are a maladaptive pattern of substance use manifested by three or more of the following, over the same 12 month period: (1) Taking larger amounts; (2) unsuccessful efforts to cut down; (3) over-investment of time; (4) giving up important social activities; (5) continued use despite negative consequences; (6) tolerance (greater need); and (7) use to avoid unpleasant withdrawal symptoms. The key features of an addiction are therefore a combination of clinical impairment, loss of control, tolerance, and a withdrawal syndrome when the substance is discontinued.

Such symptoms have a biological basis, linked to the physiology of the brain stem responsible for motivation. The loss of control that accompanies addiction is mediated, in part, by operant conditioning or instrumental learning in the mesolimbic dopaminergic pathway, which connects the nucleus accumbens with the ventral tegmental area in the mid-brain. Positive re-inforcement involves linking

an association between a behaviour and a positive reward, making the drive to perform the behaviour subconscious — e.g. smoking and experiencing a 'hit' from nicotine. Negative re-inforcement is the opposite — a rewarding behaviour that avoids negative stimuli, such as the unpleasant withdrawal symptoms that accompany tobacco abstinence in dependent smokers. Negative re-inforcement may not be linked to discomfort — even the threat of withdrawal can prompt compulsive behaviour to avoid such unpleasant consequences.

Drugs of addiction may influence dopamine concentrations in the nucleus accumbens (e.g. cocaine and amphetamines block re-uptake of dopamine in the nucleus accumbens; and opioids, nicotine and alcohol increase the firing of neurones in the ventral tegmental area, which in turn, release dopamine into the extracellular space in the nucleus accumbens). Balfour describes nicotine effects on two parts of the nucleus accumbens — the core and medial shell, which have separate effects on behaviour [13]. Increases in dopamine concentration in the core result in physiological reward, making the behaviour more likely (e.g. puffing on a cigarette). The shell is thought to mediate stimulus-response ('Pavlovian') type behaviour, so that both the behaviour itself and sensory stimuli linked to the behaviour are rewarding. Such pathways help explain why environmental cues can lead to subconscious urges to take the drug. In addition to influences on motivation, normal cognitive function declines when cues are shown (such as a smoker seeing a lit cigarette), manifest by increased time to complete modified-Stroop tests (a simple, measurable test of cognition) compared to controls [15].

Evaluation of the hypothesis — does consumption of high GI food show features of addiction?

Firstly, the same neural circuitry, linked to other addictive drugs (described above), is linked to appetite. In slow positron emission tomography (PET) studies, eating stimulates neural activity in the mesolimbic dopaminergic pathway, known to mediate cocaine and nicotine addiction [16]. Reduced dopamine (D2) receptor availability is strongly correlated with increased body mass index (Pearson correlation coefficient 0.71), indicating that increased dopamine levels are found in such regions of the brain. Low levels of free D2 receptors have similarly been reported in individuals addicted to cocaine, opiates and alcohol. Volkow et al. [11] have summarised the similarities between the neural mechanisms underlying obesity and drug addiction, and even advocated that obesity be included as a specific subtype of addiction in the new version of the DSM (V) [17].

In addition, appetite and smoking are directly linked. Restricting energy intake increases cigarette consumption [18], and restricting food intake while trying to stop smoking is linked to an increased risk of relapse [27,28]. Smoking acutely reduces hunger [29,30], and in some studies has been found to decrease the consumption of sweet tasting foods [19]. Hunger is a symptom of nicotine withdrawal and people may gain an average of 3.5 kg from stopping smoking [20].

Furthermore, high GI oral glucose reduces urges to smoke and other tobacco withdrawal symptoms [21]. Glucose may alleviate the urge to smoke by satisfying the need for carbohydrates and satiating appetite. The link between appetite and smoking is not well understood. West [21] suggested that glucose may effect withdrawal relief through a complex pathway involving serotonin, tryptophan and insulin. Nicotine, like other drugs that stimulate serotonin release in the brain [22], reduces appetite. Serotonin production depends upon tryptophan, and the entry of tryptophan into the brain is indirectly influenced by glucose ingestion [31]. Rises in plasma glucose, from carbohydrate, increase plasma insulin levels that lower blood large amino acids that compete with tryptophan for uptake into the brain. Thus reduced plasma concentration of large amino acids causes increased uptake of tryptophan into the brain, and raises serotonin levels, suppressing appetite and the desire to smoke.

The biological circuitry may be similar for food as with nicotine and other drugs of addiction, but are the symptoms similar? Strong evidence links automaticity to eating behaviours. Several mechanisms influence consumption that are not consciously controlled. Increased portion size predicts greater food consumption (per meal), independent of body weight [23]. Also, reduced effort to access food has been linked to increased consumption. In one study, subjects consumed 5.6 more chocolates per day if the chocolates were situated at their desk, rather than on a shelf two metres away [24]. In another study, subjects that were provided continuously refilled bowls of soup consumed 73% more soup, than controls [25]. Such evidence suggests that, the sight of food may stimulate over consumption by a Pavlovian stimulus-response, observed with other addictions. The importance of the food environment, tested here by measuring variation in food availability, portion

size and cues to eat caused changes in consumption behaviour in controlled conditions. Such environmental influences on food consumption suggest that loss of control — a key element of addiction — is present.

The negative health consequences caused by obesity, along with the social stigma are likely to fulfil the requirements in the DSM IV for impairment and distress. Obesity results in a range of diseases, including premature death, cardiovascular disease, type-2 diabetes, hypertension, obstructive sleep apnoea, osteoarthritis and social isolation. Such is the link between obesity and mortality, high body mass index is globally ranked seventh leading cause of death [2].

Other features of addiction, such as a withdrawal syndrome, are not commonly described for eating. However, anecdotal descriptions of such syndromes exist. Atkins' [12] describes a real estate executive who is unable to lose weight despite emetics and laxative use, or even obesity surgery. The executive recalls *''often I would shake until I could put some sugar in my mouth''*. Cues are also described — *''I had an hour's drive from my office to my home, and I knew every restaurant, every candy machine and every soft drink dispenser along the whole route.''* Although this may be an extreme example, subtle symptoms similar to those of nicotine withdrawal, such as irritability, poor concentration, and urges may accompany abstinence from high GI food, and may be underrecognised, as often the threat of such symptoms may prompt subconscious drives to perform the addictive behaviour.

The key element of our hypothesis relates food addiction potential to GI. Support for this idea is drawn from parallels to what is known of nicotine dependence and the pharmacokinetic properties of nicotine delivery devices. Time to peak arterial concentration of nicotine predicts the addictive potential of a delivery device, with a cigarette providing the ultimate in fast delivery with peak concentrations delivered to the smoker's central nervous system within seconds of inhaling [26]. Nicotine replacement therapy (nicotine gum, patch, inhalator or nasal spray), in contrast, has a slower profile, with the time to peak concentration of nicotine gum between 30 min and 60 min. The addictive potential of such products is lower, and so provide a step, partially reducing nicotine withdrawal symptoms in recovering smokers, and roughly double the chance of quitting [27].

Glycemic index, although describing the average rise in plasma glucose, is also linked to time to peak concentration of plasma glucose — like nicotine — so that high GI foods have a short time to peak concentration. However, time to peak glucose concentration may be affected by factors other than GI which may have an effect on the mesolimbic dopaminergic system, such as fat, caffeine and various amino acids. Foods with other addictive agents may be more re-inforcing than predictions made from the GI alone, such as Coca–Cola®, which contains high levels of both sugar and caffeine. Taste may also be an important reinforcer.

Consequences of the hypothesis for public health policy and treatment of obesity

If GI is a predictor of the addictive potential of food, what are the consequences? How could this help to reduce population obesity prevalence? Current population health interventions are primarily aimed at reducing the overall energy content of food. Some sections of the food industry have followed such demands by reducing the total fat (and energy) content of their products. Often the carbohydrate content of such foods increases as a result. If our hypothesis is correct, these foods may be more re-inforcing of overeating behaviour than those they have replaced.

To further support the contribution of food addiction to global obesity, in the last fifty years, high GI sweeteners have been a growing part of the world's diet. Popkin et al. reviewed disappearance data of caloric sweeteners from 103 countries in 1962 and 127 in 2000 [28]. More detailed assessment of interval time trends were made in the United States. World wide — 32% more kcal/capita/day of sweetener was consumed in 2000 (306) compared to 1962 (232). In the US, such a rise is mainly due to increased consumption of soft drinks, with per capita calories consumed from such products increasing from 52 kcalorie/day in 1977 to 105 in 1996 — a rise of 102%! This trend may reflect increasing individuals with addiction to high GI drinks and/or greater consumption or tolerance to such products.

Such understanding of the mechanics of addiction has lead to specific public health action. Tobacco control advocates have argued for regulation of tobacco displays because such advertising may act as a cue and so prompt relapse in smokers making a quit attempt [29]. The parallel from tobacco smoking to food consumption is evident, however, nicotine and cigarettes are now accepted as causing addiction, whereas food addiction is not widely understood or known, so

parallel arguments to control food related cues have not been effectively applied.

If high GI food is the villain by virtue of reinforcing properties, low GI equivalents may be a saviour. Just as slow release forms of nicotine help smokers recover from addiction, low GI foods may reduce cravings in obese or overweight populations. Substituting high GI food for low GI equivalents (eg. white bread for wholegrain bread in place of white bread), may reduce craving and improve control of obese persons over their food choices and weight. When helping smokers quit, often they must be convinced to use enough nicotine replacement therapy to assist them to overcome cravings, reassuring them that such use will ultimately help them quit smoking altogether. This is where our theory diverges from low carbohydrate diets advocated in the popular press. Such diets (e.g. the Atkins diet) advocate extreme carbohydrate restriction (no more than 20 g per day in the 'induction phase' cf. FDA daily recommended value of 300 g for a typical 8,400 kilojoule per day diet). This approach is equivalent to quitting smoking 'cold-turkey', and is likely to be associated with a low chance of successful behaviour change (e.g. <5% one year abstinence rate for smokers quitting cold-turkey [20]).

Other parallels with nicotine addiction may be drawn. Smokers' level of addiction and predicted success stopping smoking can be assessed using measures of dependence that correlate to measures of daily nicotine exposure, (e.g. the Fagerström Test of Nicotine Dependence and serum cotinine, respectively). Similarly, a measure of daily glycemic load may predict the level of food addiction or tolerance to carbohydrate, and be of prognostic significance when tailoring clinical interventions. Evidence of tolerance for total carbohydrate intake in a population may be seen in the dramatic increase in serving size over the last thirty years in the United States [30].

Many factors may influence the glycemic index of food, such as starch gelatinisation, physical entrapment of starch, high amylase to amylopectin ratio, particle size, viscosity of fibre, sugar type, acidity (through effects on gastric emptying) and fat content [5]. Such properties may be manipulated during food manufacture to produce subtle changes in glycemic index, without significantly changing taste. If our theory is correct, and significant changes are made to carbohydrate foods that are consumed in large volumes (such as breads and cereals), the potential for public health gain is large.

Just as measures to control the tobacco environment have proved most effective at reducing the prevalence of smoking, similar strategies may help reduce the obesity epidemic. Cues, such as advertising, that show repeated images of individuals consuming high GI foods may reduce control in conditioned individuals. Children may be particularly affected by such stimuli. This theory adds impetus for legal control of food advertising. Similarly, cost measures (e.g. tax increases) have proven useful in prompting quit attempts and reducing tobacco use. This strategy applied to food (e.g. a high GI food tax) may reduce addiction at a population level.

Conclusion

We have discussed the evidence that food consumption shows similarities to other addictive behaviours and that GI may be the element of food that, like nicotine in cigarettes, predicts its addictive potential. Further, direct links between appetite, glucose ingestion and tobacco withdrawal symptoms are described. Empirical scientific and clinical studies support an addictive component of eating behaviour, with similar neurotransmitters and neural pathways which may be triggered by consumption of high GI food, as with other addictive drugs. The importance of regulation of the food environment to control subconscious behaviour prompted by cues is again emphasised. However, subtle changes in the preparation of commonly consumed food items, reducing glycemic index, possibly through regulatory channels, may reduce addiction and confer large public health benefits. Although parallels with nicotine addiction and food/GI are drawn, differences exist. Food is necessary for survival and 'the tiger cannot be put away in a cage' [1] can not be put away in a cage. However, study of factors that provoke the 'tiger' may protect individuals and populations from the harm it causes.

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