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'The hunger trap hypothesis': New horizons in understanding the control of food intake

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A B S T R A C T

The global obesity epidemic continues to present significant challenges to individuals and healthcare providers. Public health initiatives to tackle the rise in overweight and obesity in developed and developing nations have largely failed to tackle the problem and research into the underlying causes is of increasing importance. Central to understanding overconsumption of calories is an appreciation of the mechanisms of hunger and satiety. Research to date has revealed considerable detail regarding meal size, macronutrient composition of the diet and control of energy balance via adipose store derived signalling. It is clear however that such control mechanisms are overwhelmed in a significant proportion of the population. We hypothesize the hitherto under-researched possibility that micronutrient status may have an important role in energy balance. Poor vitamin and mineral profiles in the diets of the obese may potentiate overconsumption of calories due to an insufficiency of micronutrient intake relative to macronutrient consumption, a situation aggravated by increased requirements in the obese state. Amongst the multiplicity of metabolic and biochemical processes dependent upon micronutrients and which are impacted by their relative insufficiency, there may be triggers for increased food consumption in an attempt to bridge the gap between high energy consumption and low co-factor availability. This 'hunger trap' will continue as long as low nutrient density foods represent the mainstay of the diet. The accepted paradigm of variety seeking leading to vitamin and mineral adequacy of diets may not apply in the context of highly processed foods which use technological means to mimic organoleptic properties of nutrient density without delivering the same at the level of metabolism.

Main body

The global obesity epidemic and associated pressures on healthcare providers are showing little sign of abating [1–3]. Public health initiatives and pharmacological approaches to the problem have made little impact on the rising tide of overweight and obesity in developed, and increasingly developing, nations. This situation necessitates a better understanding of the factors promoting positive energy balance in individuals and populations. While science and medicine may inform the debate in terms of increased knowledge and understanding of the issues involved, to date the perspectives arising from research and clinical practice have failed to stem the rise in obesity. The constellation of factors driving the obesity epidemic range from the social and economic through to genetic [4,5]. Discussion around obesogenic environments and economies, thrifty genotypes and epigenetics, and the roles of educators, individuals and politicians can be found aplenty in the mainstream and scientific media. The present paper will explore one perspective which seems to have received little attention. We hypothesize herein that micronutrients may be intimately involved in the control of energy balance in man and that dysregulation of micronutrient dependent systems may be a significant factor determining a dysregulation of energy balance homeostasis.

With respect to the control of food intake per se, there is a long history of research which has yielded tremendous amounts of information in terms of the short and longer-term regulation of the intake of food and the expenditure of energy [6,7]. From the glucostatic [8] and lipostatic [9] theories, the study of meals as units of food intake, the roles of gut and adipose derived peptides in signalling to the central nervous system about the immediate and longer-term state of nutrient flow and storage in the body, we now have in many respects, a detailed picture of the key determinants of hunger, satiety and energy balance homeostasis [10]. Hunger and appetite, as the means to ensure the ingestion of those dietary elements that are required to sustain life, being central to these perspectives. However, while calorie and macronutrient intake have to date been the focus of the study of food intake control, very little work has examined the role of micronutrients in the complex of physiological processes determining the nature and quantity of food consumed. Aside from the observation of 'variety seeking', there is little information available to help conceptualize how requirements for the wide range of required micronutrients are met.

If macronutrient sufficiency is achieved through quantitative and qualitative food selection behaviours, then it is rational to conjecture that there may be mechanisms in place to ensure adequate micronutrient status also. Vitamins and minerals are no less essential in

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dietary terms, than essential fatty acids or essential amino acids, raising the question as to how the body maintains sufficiency in the apparent absence of micronutrient-specific hunger[s]. Craving sodium in salt, and the poorly understood Pica phenomena are the only know drives for micronutrient ingestion specifically [11,12]. In this connection, the drive for variety in foods eaten, macronutrient-cycling, and sufficiency in terms of quantity, is thought to be the means by which vitamin and mineral needs are met. Indeed, this makes for an interesting starting point from which to explore the idea that obesity may in part at least be driven by processes designed to maintain physiological and biochemical integrity in the whole organism.

Many studies have shown that, in the human obese state, body micronutrient status is poorer than in the non-obese state [13,14]. Interestingly, intake studies also show that the obese consume diets with lower (micro)nutrient density than their lean counterparts [15]. In addition, vitamin and mineral supplement takers have on average lower BMIs than those who do not take supplements [16]. Furthermore, in the few studies that have been carried out in this area [17–19], the provision of micronutrient supplementation has been found to assist with weight loss compared to non-supplementation. Taken together, these findings suggest that there may well be a hitherto underreported relationship between micronutrient status and energy balance. The basis of the present argument therefore, is that 1) poor micronutrient status can in fact be 'sensed' and 2) the means to address this is enacted as increased overall food consumption.

It is important to examine the key questions raised by these possibilities. Firstly, what may be the mechanism by which micronutrient status is 'sensed'? The lack of receptor – effector homeostatic feedback loops to regulate vitamin and mineral levels in the body, (particularly the lack of micronutrient receptors apparent in the gastrointestinal (GI) tract) is probably the reason for the lack of research in the area. However, if the range of processes, pathways and functions that are micronutrient dependent are considered, a different picture emerges. For example, ATP synthesis, neurotransmitter formation, hormone production and action and a multiplicity of anabolic and catabolic pathways and processes are directly and indirectly reliant upon micronutrients as direct agents of action or enzymatic cofactors [20]. Viewed in this way, 'sensitivities' to micronutrient insufficiency may be envisaged. For example, there are many neurotransmitter systems involved in the control of hunger, satiety and eating behaviour and while little surprise ensues when pharmacologic manipulation of these systems leads to increased or decreased eating behaviour, we have little understanding of the potential impact that the relative availability of vitamins or minerals may have on the same systems, despite their known dependence on micronutrients for proper function. Equally, while rates of cellular ATP production or glucose utilization or hepatic glycogen synthesis or fatty acid utilization are acknowledged to impact on eating and hunger at whole organism level, we have little 'feel' for the impact of the relative availability of micronutrient cofactors which are essential for these bioenergetic and metabolic processes [21]. If a changing status of substrate flux, metabolite accumulation or neural activity can signal hunger or satiety, it is reasonable to ask whether the sufficiency or otherwise of the micronutrient elements which support the same, might be considered as factors involved in the regulation of energy balance. The lack of specificity with respect to exactly which from the list essential vitamins and minerals might be involved is perhaps currently of less significance than the response to any deficit – if that response is to eat more food.

This takes the hypothesis to the second element, i.e. having 'sensed' micronutrient insufficiency, the remedial is to eat more food, even if absolute energy balance is positive. That is, hunger elicited by relative micronutrient deficiency may persist even when body fat stores are more than adequate. In such a scenario, it is tempting to speculate that a nutrient deplete diet encourages overeating inasmuch as the metabolic processing of the food eaten requires micronutrient, which if not present in sufficient quantities in the diet, could lead to further hunger, as the deficit is sensed and the means to overcome micronutrient deficit is to prompt hunger and eating. In addition, the obese state in and of itself, increases requirements for micronutrient, which may then further potentiate eating behaviour through the same mechanism.

Many obese individuals report hunger as a significant barrier to eating less and indeed the obese appear to subjectively experience hunger more profoundly than lean counterparts, despite plentiful energy stores [22]. It is possible that this phenomenon is in part at least driven by an attempt to 'catch up' the differential between macro and micronutrient dietary supply. Given the evidence base regarding the typical nutrient density of the diets of the obese compared to lean individuals and the increased micronutrient requirements of the obese, it follows that the hypothesis that nutrient dense diets are protective against obesity is worth testing. A lack of precise mechanistic understanding of the mechanisms by which vitamins and minerals may modulate food intake and energy balance should not preclude the first step of investigating the precise vitamin and mineral content of the diet with respect to energy balance in man.

It is important at this stage to include in this model, the concept of a set point in energy stores and understand the potential influence of micronutrient status on energy balance around such a set point. The discovery of leptin and its role in modulating energy intake and expenditure has lent weight to the notion that fat stores are indeed under some form of homeostatic control [23]. Clearly such a control mechanism can be deranged (as is the case in obesity). However, it remains a truism that many people remain within a remarkably narrow weight range for long periods of time while paying little or no attention to their calorie intake. It appears therefore that there is indeed a mechanism to remain in an approximation of energy balance but that in many individuals this is capable of being overwhelmed when confronted with an obesogenic environment.

This all begs the question as to what obesogenic factors are causing the dysregulation of homeostatic control and what if anything can be done to remedy the situation. In the case of the sparse, but consistent indications from the extant literature regarding the impact of micronutrient density of food on energy balance, it is rational to explore the premise that micronutrient deplete diets may encourage the dysregulation of energy homeostasis in man [24].

While there is data in the extant literature to suggest that increasing the micronutrient density of the diet may reduce hunger acutely and fat stores over time, there is the curious case of micronutrient deficiency in the underweight seemingly reducing hunger levels rather that increasing them. In such cases it is a consistent clinical observation that the provision of supplemental vitamins and minerals will encourage rather than discourage overall food intake and provide an assist in restoring the overall nutritional status of the affected individual [25].

To understand how micronutrient provision may reduce hunger in the overweight state yet increase hunger in the underweight state, we can consider the following evolutionary argument. The accepted paradigm of human metabolic responsiveness to food supply, often referred to as the biology of 'feast and famine' [26], acknowledges a human prehistory in which access to nutritious food may have been a variable affair. At times there may have been a glut of nutritious food, whilst at other times there may have been little of nutritional value available [27]. As such, the behavioural response to the changing nutrient opportunity landscape would have been as important as the metabolic response. That is, when good [nutrient replete] food sources became available, it would have been important that eating behaviour was elicited and sustained until repletion occurs.

In the context of a valid contemporary scenario we might envisage an individual with psychological problems, a disease or a drug addiction, who for some time has eaten poorly in both qualitative (nutrient density) and quantitative terms [protein and energy] and is in effect undernourished and malnourished. Such individuals frequently respond with increased hunger and food intake, when given a multi-vitamin/mineral supplement. This supports the notion that when 'cue' for a

nutritional opportunity has been stumbled across, that feeding behaviour should be increased (at that point in time) to exploit the situation. The inward flux of micronutrients that supplement provision gives to those in the clinically induced underweight state could then help restore the many biochemical pathways dependent on micronutrients and allow a shift towards restoration of homeostatic control mechanisms of energy balance via the hunger system. This common example is based around low BMI situations, which are frequently caused by problems, either psychological or otherwise clinically based, that an individual may encounter [28]. Non-pathological states, for example athletes with a lower end BMI profile, seldom present with issues of blunted hunger/appetite, and generally enact nutritionally sound (nutrient dense) food choices. No additional food intake is elicited through micronutrient supplementation in such cases.

We have described one end of the energy balance spectrum [underweight], with an evolutionary basis to describe the positive effects of micronutrients on food intake, so we must now explore the case of overnutrition. We hypothesize a different, but nevertheless micronutrient related mechanism, that we have termed the 'hunger trap' is at work in the case of obesity. In this model, the potential role of micronutrients in allowing the homeostatic defence of the adipose mass 'set point', is examined. Observations of lower micronutrient densities in the diets of the obese, altered food preferences, reports of steadily lowering micronutrient soil [29–31] and plant levels [32–34] and the known increased micronutrient requirements in the obese state [35–37], deserve proper consideration in the puzzle of the causes of the inexorable rise in obesity rates over the last 50 years [38], which remain unresolved by existing public health initiatives.

While there is currently little information available in terms of elucidated mechanisms underlying the role of micronutrients in energy balance, an example might be found in the case of ascorbic acid (AA; vitamin C) which may differentially affect hunger/satiety in the case of both low and high body fat stores.

Obesity has been shown to be associated with low plasma AA status [39–41] and a negative correlation exists between BMI and AA status [42]. AA has been shown to reduce plasma leptin in a dose dependent manner [43,44] which in the underweight state is appropriate, having the effect of increasing hunger and feeding behaviour. In the obese state this effect may seem undesirable, until one considers the problem of leptin resistance in man which is driven by persistent elevations in circulating leptin levels [45,46]. A diet high in ascorbic acid could therefore be advantageous, as over time a key determinant of leptin resistance would be attenuated. Additionally, ascorbic acid has been shown to inhibit the hypertriglyceridemia of obesity. This is significant as elevated plasma triglycerides are implicated in the inhibition of leptin transport across the blood brain barrier [47], a phenomenon which is now thought to underpin the development 'leptin resistance' [48]. Taken together, such effects could indicate how vitamin C might be involved, via leptin signalling in modulating calorie intake.

Another micronutrient that has presented tantalizing snippets of research information in terms of energy balance is calcium. The majority of observational studies in this connection report inverse relationships between body fat mass and dietary calcium intake [49–51]. In a prospective study of calcium (plus vitamin D) supplementation, modest weight loss over a three year period was noted and perhaps equally importantly, in those not losing weight, protection against weight gain was observed [53]. While some of the data in this regard only shows relatively small effects of calcium alone, it is interesting to note that in a study providing calcium in the form of a calcium/potassium salt of hydroxyl-citric acid produced consistent reductions in body weight and large reductions in serum leptin (38%) and increases in serum serotonin of some 44% [52]. These findings suggest that future research into micronutrient influences on energy balance should include combined as well as single nutrient perspectives. It seems likely that research into the whole array of known essential micronutrients and their potential combinations, could reveal many ways (direct and indirect) by which hunger, satiety and feeding behaviours might be affected. Given the lack of published data in these areas, there may still be a long investigative road ahead of researchers.

Conclusion

To summarize the basis of the 'hunger trap', those neural, hormonal, neuro-hormonal, and metabolic processes that may be influenced by micronutrient availability or flux, may in turn influence increased or decreased food intake behaviours. In the context of an obesogenic environment, where the advertising and availability of high calorie, easily affordable but relatively (micro)nutrient 'light' foods are ubiquitous, the ingestion of such foods has increased considerably over the duration of the obesity epidemic. The assumption that obesity flourishes in an obesogenic environment simply because calories are easily available, does not address the mechanism[s] of derangements in hunger and satiety that allow consistent overconsumption to occur, or why some individuals are affected whilst others are not. Considering then energy unbalance in terms of obesity, qualitative aspects of diet may in fact be crucial. High energy, low nutrient density diets are central to the 'hunger trap hypothesis' as the constant inflow of calories, largely unaccompanied by factors required for their proper employment, will compromise, or alter, multiple biochemical and metabolic processes relating to energy balance homeostasis [54]. Given the multiplicity of cues for eating, both physiologic and psychosocial, it is unsurprising that in the absence of qualitatively sound nutritional options, hunger can persist beyond caloric sufficiency.

It is interesting to consider the timeline of the obesity epidemic with respect to dietary habits, trends and norms that accompanied the rise in rates of overweight and obesity. The present hypothesis would suggest that since the 1970s there has been a decline in micronutrient density of foods commonly eaten [55–57]. But was this the case? Certainly, there has been a documented decline in soil and plant matter levels of minerals across this time-period. The magnitude of the decline may not however be sufficient to account for the rises in obesity levels that have occurred. Additional relevant factors could include a decline in the consumption of nutrient rich organ meats and in the range of plant matter eaten, an increase in the consumption of food eaten outside the home; a reduction in home meal preparation that has occurred with changing social and economic roles and the increased popularity of highly productified food items. Alongside these phenomena, the visibility, frequency and sophistication of food product advertising has increased dramatically since the 1970s and it is difficult to imagine that this has not had effects on the eating habits of those exposed. The obesogenic triggers and predisposing social and economic factors that conflate to influence food choices appear to have particularly impacted the lower socioeconomic and educational sectors of society, who in turn have been the most affected by the obesity epidemic [58].

There is another nutritional phenomenon that has played out through the same decades that have seen the rise of obesity levels, namely the dogma of dietary fat as a 'bad food choice'. With its principle origins in the work of Ancel Keys [59,60], the notion of fat as a risk for cardiovascular disease and obesity gained almost total acceptance within clinical and public health thought and practice through the 1960s and by the 1980s little alternate discourse had a serious place in mainstream science and medicine. Dietetic and public health education and information programs emphasized [and for the most-part still do] the need to reduce fat intake [61,62]. The response of the food industry was to design and market products with reduced fat content. To maintain palatability there was an increase in the content of carbohydrate, mostly in the form of refined sugars (sucrose, glucose syrup, high fructose corn syrup). Despite reductions in average fat consumption in much of the developed world since the 1980s [63,64], the rise in obesity did not abate, rather continued alongside reduced fat consumption [64,65].

Foods high in fat, meats and organ meats, oily fish and dairy

produce are generally of considerably higher nutrient density than refined carbohydrates. Refined carbohydrates in the form of sugars, white flours, refined cereals/grains, white rice and potatoes, deliver relatively little vitamins and minerals [66,67], yet have been recommended by nutrition advisory committees at national levels, to represent 50% or more of daily dietary energy [68,69]. Refined carbohydrate consumption produces reward responses in the brain and are such food items are highly palatable [70] being amongst the few innately preferred tastes. The trend to replace fat with carbohydrate correlates with the rise in obesity over the past few decades [71,72], and increased carbohydrate consumption is increasingly implicated in the metabolic derangements associated with obesity.

It seems fair to assume that factors which increase product (food) purchasing and consumption behaviours are attractive targets to purveyors of the product. In the case of highly refined, hyper-palatable foods, ratios of carbohydrate to fat known to elicit maximum CNS reward responses have been argued to bestow addictive potential on the food item [73]. This assertion is supported (in animal models at least), by observations that drugs used to treat addictions may have utility in the treatment of overeating/obesity [74]. The dual challenge of micronutrient co-factor deficit and addiction related induction of changes in neural architecture and function, could produce a 'perfect storm' of factors which continually encourage food intake and overwhelm satiety signalling. An evolutionary mismatch has arguably emerged, between neural systems promoting reward and repetition of eating behaviours, advantageous to our Palaeolithic antecedents but both unsuited to and increasingly exploited in the industrial present [75].

In the context of replacing fat with carbohydrate, it is also of interest that concerns about the level of sugar consumption have more recently led to the increasing use of low or calorie free artificial sweeteners in a wide range of food products [76]. Ironically, given the reduction in energy intake that using such products brings about, there is increasing evidence suggesting that artificial sweetening agents may aggravate obesity through disconnecting post-ingestive metabolic events from the organoleptic properties of the food eaten [77,78]. It may be in fact, that resistance to satiety hormones, such as leptin and insulin, in obesity, represent adaptive mechanisms, which prevent the induction of satiety when playing 'micronutrient catch-up' to an exaggerated macronutrient surplus. Recent research demonstrates that in the UK and US some 50% of food purchases are of highly processed, refined foods, rich in carbohydrate and sweeteners and often low in micronutrients [79]. Such foods are disproportionately represented in the shopping baskets of those in lower socio-economic strata [80] the same demographic that is disproportionately affected by obesity [81].

Given the innate drive for variety in food selection [82], it is noteworthy that many food products utilize colorants and flavourings, and textures, which give the appearance of nutrient variety despite being the same (consider well-known brands of sweets/candies, all the same but in multiple different colours and flavours, and micro-particulated proteins which give 0% fat yoghurt a creamy texture). Hardwired evolutionary drives for variety [83] may be at least partially satisfied at organoleptic level, with such products, but the downstream metabolic and neurochemical processes dependent upon the suggested but absent nutrient profile of the foods eaten are not [84,85]. The hunger trap continues as the mismatch between calories and micronutrients proceeds, with continued hunger as the inevitable result.

We accept that diseases commonly seen at low BMIs are frequently the cause of the low BMI [86] while diseases seen at high BMIs are most often caused by the excess fat stores [87]. We might extend this perspective then to the drivers of unbalanced energy consumption itself. Low levels of food intake being caused initially by pathological physical or psychological states and excess food consumption being driven by the ingestion of foods that 'masquerade' as micronutrient providers. The challenge in either scenario being to 'reset' or sensitize the set point in order that food consumption matches requirements and does not fall short of or exceed them. Studies that examine the food habits of people who do not have problems maintaining a healthy weight, generally find that the nutritional profile of their diets represents a good balance of macro and micronutrients [88,89]. That is, the nutrient profile of the foods eaten supports not only the energy demands of the individual, but also the myriad of biochemical and metabolic processes that accompany and facilitate the energy in–out axis. A shortfall in cofactors for all or any of these processes eliciting compensatory behaviours and hunger will remain, as long as the mismatch between macro and micronutrient intake persists.

While any individual component of the present argument may be insufficient to fully account for the obesity epidemic, the sum of these parts could explain the observed rise in obesity over the past 50 years across large sections of many populations globally [90–92]. The argument also holds true for those apparently unaffected by overweight, ie those people eating nutrient dense and largely unprocessed foods, who demonstrate apparent homeostatic control over fat stores. We should therefore now extend our thinking and research to explore how dysregulation in homeostatic control of energy balance might be brought about by consuming micronutrient deplete foods and foods which suggest but do not deliver micronutrients in proportion to macronutrients.

Declaration of Competing Interest

We declare that there are no matters of conflict of interest. No funding was received for this article; we did not receive any sponsorship.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2019.109247.

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