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COMPLEMENTARY HYPOTHESES ON CONTRIBUTORS TO THE OBESITY EPIDEMIC

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Abstract

Increased rates of obesity have occurred within virtually every race, age, sex, ethnicity, and economic group. Despite substantial punditry on the issue, the exact reasons are incompletely known. The two most common factors cited as contributing to the obesity epidemic and those whose causal influence on increasing obesity levels in the population are often presumed unequivocally, are food marketing practices and institutionally-driven reductions in physical activity. Previously, we have taken to calling these “the big two.” In this commentary, we build on previous writings in this area to introduce additional factors that may contribute to the obesity epidemic. Here we simply emphasize that there may be other factors working in combination with “the big two,” influencing body fatness through effects on energy intake, energy expenditure, and/or nutrient partitioning.

Keywords

Diet; Energy Balance; Physical Activity; Weight Gain

Introduction

Most readers have witnessed the profoundly increased prevalence of obesity illustrated on CDC maps. The two factors most commonly cited as having an unequivocal, causal influence on population obesity levels are food marketing practices and institutionally-driven declines in physical activity. Previously, we labeled these “the big two.” Here we update our previous writings and introduce other putative contributors.

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Our questioning of “the big two” as the sole causes of obesity in no way dismisses them as contributors to population obesity levels. We simply emphasize that additional factors may be involved, and expand on current evidence for each in Table 1. We also emphasize the importance of not conflating “the big two” with energy intake and energy expenditure. The laws of thermodynamics are not in question and we maintain the belief that changes in body energy stores, largely manifested as changes in body fat, result from the difference between energy intake and expenditure. Thus, “the big two” almost assuredly influence adiposity.

Good scientists simultaneously maintain both healthy skepticism and open-mindedness. Hence, we are open to speculation and conjectures on many “outside the box” contributors. We also recognize that speculation and conjecture are not proof, and we and the reader should remain skeptical concerning the extent to which these factors impact obesity.

Behavioral Factors

Sleep Debt

Behavioral factors change with culture, environment, and technology. Over the last several decades, Americans have been sleeping less[1]. In both model organism studies and short-term human experiments, sleep deprivation affects energy intake and expenditure[1,2]. Over long periods, this can lead to increased adiposity. Conversely, helping individuals sleep more might attenuate weight gain. Randomized controlled trials testing such interventions are necessary and underway.

Decreased Smoking

Cigarette smoking and nicotine have anorexigenic effects and increase resting metabolic rate[1]. Generally, individuals who quit smoking gain weight. Thus, decreased smoking rates in the last half-century likely contributed to the obesity epidemic. Nevertheless, we emphasize in the strongest possible terms that the negative health effects of smoking are profound and we recommend continued smoking cessation.

Environmental Exposures

Increased Atmospheric CO_2

A creative hypothesis in the early exploratory stages concerns rising atmospheric CO_2 levels. CO_2 has been documented as a contributor to oceanic acidification and may similarly shift organismal pH. Reductions in pH are sensed by neurons within the lateral hypothalamus, leading to secretion of orexin, which promotes wakefulness and increased energy intake[3]. Combined with increased feeding, the effects of orexin on arousal could promote sleep debt and subsequent weight gain.

Ambient Temperature

Thermoneutrality refers to the ambient temperature at which the energy required to maintain core body temperature is minimized. Human and animal studies have shown that exposure to temperatures above or below this zone result in increased metabolic rate, and therefore potential weight reduction[1,2]. Over the last 30 years, use and efficiency of home heating and

cooling systems has risen, and vocational work requiring environmental exposure outside thermoneutrality has declined, potentially leading to weight gain[1].

Technology

Use of electronic media and technology has increased, particularly among children and adolescents. Greater screen time is associated with increased appetite, reduced physical activity, and higher obesity rates[4].

Suspected Endocrine Disruptors

Manufactured chemicals hypothesized to disrupt endocrine function have increased in the environment, the food chain, and humans[1]. These substances include commonly used plastic-hardeners, pesticides, solvents, heavy metals, and phthalates. Binding of these chemicals to nuclear receptors for estrogen, PPARγ, and retinoic acid X may increase adiposity by promoting adipocyte differentiation, which could lead to increased rates of obesity in the presence of positive energy balance. Additionally, certain chemicals may dysregulate lipid metabolism or act as antiandrogens, resulting in increased fat deposition[1,2].

Pharmaceutical Iatrogenesis

The use of pharmaceuticals known to cause weight gain (psychotropic medications, antidiabetics, antihypertensives, steroid hormones and contraceptives, antihistamines, and protease inhibitors) has drastically increased[1,2]. In fact, the incidences of diagnosed anxiety and depression, type 2 diabetes, and hypertension, along with associated medications, match climbing obesity rates.

Infections

While conflicting results exist, adenovirus 36 (Adv36) and other microbial infections have been associated with human obesity. In both cell culture and model organisms, Adv36 infection accelerated the differentiation and proliferation of preadipocytes into lipid-laden adipocytes[2].

The Gut Microbiome

Multiple mechanisms have been considered to explain how dysbiosis of gut microbiota may be involved in obesity. Excess body fat may alter populations of gut bacteria, which could impact metabolism through impaired gut signaling pathways governing inflammation, insulin sensitivity, and adiposity[5]. This is an en vogue topic, yet it must be acknowledged that cause and effect is uncertain.

Social-Psychological Factors

Economic disparity and insecurity may produce both physiological and behavioral changes resulting in increased energy intake[6]. Delay discounting, or how the value of a reward decreases as the time until reward receipt increases, has also been studied in human diet and physical activity adherence[7]. Humans typically prefer smaller immediate rewards, presenting the possibility of little value in maintaining or achieving a healthy weight. The last two

decades of research in this area have produced abundant evidence of higher reward discounting in drug-dependent individuals, gamblers, and persons prone to obesity[7]. Finally, greater cognitive demand, with resulting hyperphagia and poor dietary choices, may impact body weight[8].

Reproductive Factors

Humans assortatively mate for adiposity, and higher BMI has been associated with having more offspring[1,2]. These two factors combined would be expected to increase the frequency of genotypes susceptible to obesity. In utero, energetic factors can lead to obesogenic effects passed down over generations[1,2]. These effects could be amplified with higher gravida age, as more women delay reproduction beyond age 30[1,2]. A more recent concept is that of fetal drive, whereby the offspring's genotype drives the physiology and behavior of the mother, potentially impacting her obesity risk beyond pregnancy[9].

Conclusions

While our discussion of potential contributors to the obesity epidemic is not exhaustive, it seems likely that, not one, but a combination of factors is responsible for the increased rates of obesity. Additionally, these factors are ever-changing, requiring a multifactorial approach to reducing population obesity levels and present exciting opportunities for new discovery.

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References

1. Keith SW, Redden DT, Katzmarzyk PT, et al. Putative contributors to the secular increase in obesity: exploring the roads less traveled. Int J Obes. 2006; 30:1585–1594.
2. McAllister EJ, Dhurandhar NV, Keith SW, et al. Ten putative contributors to the obesity epidemic. Crit Rev Food Sci Nutr. 2009; 49(10):868–913. [PubMed: 19960394]
3. Hersoug LG, Sjodin A, Astrup A. A proposed potential role for increasing atmospheric CO_2 as a promotor of weight gain and obesity. Nutr and Diabetes. 2012; 2(3):e31.
4. Rosen LD, Lim AF, Felt J, et al. Media and technology use predicts ill-being among children, preteens and teenagers independent of the negative health impacts of exercise and eating habits. Comput Human Behav. 2014; 35:364–375. [PubMed: 25717216]
5. Sanmiguel C, Gupta A, Mayer EA. Gut microbiome and obesity: A plausible explanation for obesity. Curr Obes Rep. 2015; 4(2):250–261. [PubMed: 26029487]
6. Kaiser KA, Smith DL, Allison DB. Conjectures on some curious connections among social status, calorie restriction, hunger, fatness, and longevity. Ann N Y Acad Sci. 2012; 1264(1):1–12. [PubMed: 22834696]
7. Barlow P, Reeves A, McKee M, Galea G, Stuckler D. Unhealthy diets, obesity and time discounting: a systematic literature review and network analysis. Obes Rev. 2016; 17(9):810–819. [PubMed: 27256685]
8. Chaput JP, Tremblay A. Acute effects of knowledge-based work on feeding behavior and energy intake. Physiol Behav. 2007; 90(1):66–72. [PubMed: 17023010]

9. Liu N, Archer E, Srinivasasainagendra V, Allison DB. A statistical framework for testing the causal effects of fetal drive. Front Genet. 2015; 5:464. [PubMed: 25628644]

TABLE 1

Existing Evidence of Potential Contributors to the Obesity Epidemic.

Factor	Rationale	Association demonstrated in humans?	Causal evidence of weight gain in animals?	Causal evidence of effects on weight in humans?	Causal evidence of surrogate outcomes?	Can this plausibly be manipulated to reduce the obesity epidemic?
Sleep Debt[1,2]	Reduced sleep increases appetite and decreases energy expenditure. Average amount of sleep has declined among adults and children.	Yes	Yes	Some	Yes (food intake, decreased glucose clearance and insulin response, plasma leptin, plasma TSH, and increased plasma ghrelin)	Yes
Decreased Rates of Smoking[1]	Smokers typically weigh less than non-smokers, and weight gain occurs with smoking cessation. Smoking rates among American adults have declined as obesity rates have risen.	Yes	No	Yes	Yes (nicotine increases energy expenditure, suppresses food intake in animal models, increases NPY expression)	No
Increased Atmospheric CO_2[3]	May result in lower blood pH, activation of orexin neurons in the lateral hypothalamus, and increased appetite and food intake.	No	No	No	No	No
Ambient Temperature[1,2]	Thermoneutrality minimizes energy expenditure to maintain core body temperature. Time spent in the thermoneutral zone has increased with reductions in vocational and household exposure to variations in ambient temperatures.	Yes	Yes	No	Yes (ambient temperature variations shown to affect metabolic rate and food intake)	Yes
Technology[4]	Higher screen time and technology use is associated with higher obesity rates, both of which have dramatically increased with the obesity epidemic.	Yes	N/A	No	Yes (Increased food intake and choice of energy-dense foods)	Yes
Suspected Endocrine Disruptors[1,2]	Several hormonal regulatory processes impact weight gain and are altered by man-made chemicals and heavy metals. Suspected endocrine disruptors present in the body are positively correlated with BMI and adiposity. Food chain and tissue levels have increased.	Yes (results vary)	Yes	No	No	Possibly yes, but not easily at the individual level.
Pharmaceutical Iatrogenesis[1,2]	Many common medications have been shown to contribute to weight gain. Medical diagnoses and corresponding prescriptions have increased alongside obesity rates.	Yes	Yes	Yes	Yes (remodeling adipose tissue distribution)	Yes
Infections[2]	Some infections result in increased adiposity in animals. Ad36 infection is associated with obesity.	Yes (results vary)	Yes	No	No	Not for Infections per se, but

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Factor	Rationale	Association demonstrated in humans?	Causal evidence of weight gain in animals?	Causal evidence of effects on weight in humans?	Causal evidence of surrogate outcomes?	Can this plausibly be manipulated to reduce the obesity epidemic?
						vaccines and use of analogues of the infective agent's mechanisms are conceivable.
The Gut Microbiome[5]	Gut colonization of gut microbiota results in increased adiposity in rodents. Dysbiosis of gut microbiota is associated with human obesity.	Yes	Yes	No	No	Yes
Economic Disparity and Insecurity[6]	May lead to physiological, cognitive, and behavioral changes resulting in increased energy intake.	Yes	Yes	Some (e.g., the Moving to Opportunity Study)	Some	Yes
Delay Discounting[7]	Associated with impulsivity and poor food choices.	Yes	No	No	No	Unclear
Cognitive Demand[8]	May result in poor food choices, greater food consumption, and weight gain.	Yes	No	No	Yes	Yes
Assortative Mating[1,2]	Humans assortatively mate for adiposity, which has a genetic component, producing an increased risk of obesity in offspring.	Yes	Yes	Yes	No	No
Differential Reproductive Fitness by BMI[1,2]	Adiposity is in part due to genetics, and BMI positively correlates with number of offspring. BMI is at least 65% heritable.	Yes	Yes	No	No	No
Intrauterine and Intergenerational Effects[1,2]	In-utero energy imbalances like low birth weight and overfeeding may impact offspring adiposity and pass down generations. Rates of low birth weight have climbed with obesity rates since the 1980s.	Yes	Yes	No	No	Yes
High Gravida Age[1,2]	Mean pregnancy age has steadily increased with obesity rates. There is a direct association between maternal age and obesity in offspring.	Yes	Yes	No	No	Yes
Fetal Drive[9]	Fetal genotype may alter postnatal maternal physiology impacting obesity risk and outcomes.	No	No	No	No	Not with current technology.