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Variability in Children's Eating Response to Portion Size: A Biobehavioural Perspective

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Abbreviations: Energy density, ED; monozygotic, MZ; dizygotic, DZ

Introduction

An obesogenic environment refers to an environment that facilitates the risk of obesity and includes the built and food environments [1]. Obesogenic food environments, which can be found inside and outside the home, are characterized by ready availability and easy access to large portions of energy-dense, palatable foods and beverages. As children grow older and become more independent, obesogenic environments also begin to affect their food purchasing and thus consumption behavior. A recent analysis by Drewnowski and Rehm [2], which examined energy intakes in children, adolescents, and adults by food purchase location using data from the National Health and Nutrition Examination Survey (NHANES), showed that for each age group stores and restaurants (including full-service and quick service/pizza/take-out/delivery) accounted for at least 85% of total energy intake. For younger children (6-11 years), 63% of daily energy intake came from stores, 12% from quick-serve restaurants, and 10% from school cafeterias. For adolescents (12-19 years) 63% of daily energy intake came from stores, 18% from quick-serve restaurants, and 7% from full-service restaurants. Another study by Bourradaile and colleagues [3] showed that for only ~$1 spent in corner stores (i.e., average amount spent per purchase), children in grades 4 through 6 (ages 9 years to 12 years) from urban elementary schools purchased 357 kcal worth of food and beverage items. Once again, this confirms the ease with which food is cheap, available and purchased when children demonstrate their purchasing power. Children are exposed to the obesogenic food environment and food marketing strategies, including value size pricing, at a young age and may learn to associate the purchase of large food portions with better value when making food purchasing decisions.

Current estimates indicate that 31.8% of US children and adolescents, between 2 and 19 years of age, are considered overweight or obese (BMI-for-age $\geq 85^{th}$ percentile) [4]. While this

causes concern from a public health perspective, it is important to note that the majority of children (68.2%) are able to maintain a healthy weight under the same obesogenic environmental conditions experienced by all. The fact that not all children are equally susceptible to overeating and excess weight gain suggests that differences in genetic predisposition interact with the environment to determine the expressed phenotype. Data from mostly cross-sectional research point to a positive relationship between child BMI and portion sizes consumed. For example, using dietary intake data from the Continuing Survey of Food Intakes by Individuals (CSFII) and a Nationwide Food Consumption Survey, McConahy and colleagues related average quantities (expressed as portion size z-scores) of commonly consumed foods to children's body weight (expressed as percentiles) [5]. Results showed that average portion size z-scores were positively related to children's percentile body weight indicating that children with greater body weights consumed larger food portions. Similarly, when examining associations between eating behaviors and weight status of 3- to 19-year-old children and adolescents using data from the CSFII, Huang and colleagues [6] showed that meal portion size was positively related to BMI-for-age percentiles in boys 6 years and older and in girls 12 years and older. Whilst energy requirements are greater for children who have a high BMI and growth spurts may drive periods of increased hunger, selecting larger portions of foods and beverages can become learned and then expected even when weight is stable and growth is no longer driving intake.

Controlled laboratory studies which experimentally modify food and beverage portions and precisely quantify children's food and energy intakes are critical for studying children's response to portion size manipulations. These studies are also able to shed light on the individual differences in susceptibility or resistance to overeating when served large portions. Over the past decade, a series of well controlled laboratory-based studies in children and adults have advanced

our understanding of the role of portion size in determining food intake. Interestingly, in contrast to studies with adults, portion size effects in children appear to be more variable across experiments in that some studies demonstrated significant portion size effects for a specific experimental manipulation (e.g., serving method, interaction with energy density) or child characteristic (e.g., age), while others did not (**Table 1**). Explanations to account for these differences might include study design, research methods, or differences among the cohorts studied, but it is also possible that eating behaviors are simply more malleable at a young age as children's eating habits are being formed through genetic predisposition interacting with the environment [7-9]

The aim of this review is to discuss how genetic susceptibility may interact with factors in children's early environment to predispose some children to overeat when served large food portions. We present evidence for the proposal that children's response to portion size may in part be determined by innate (genetic) appetite and eating traits, which can affect meal size. We further discuss evidence for children's response to portion size as a learned behavior influenced by upbringing (parenting style and feeding practices) and early environment.

Genetic Influences Underlying Food Intake and Meal Size (Nature)

Typically, genetic susceptibility to obesity is identified through twin studies and via linkage and association studies connecting the functional role of specific genes to the expression of differences in body mass, appetite regulation or eating traits. There are multiple, complex routes to obesity, but certain behavioural traits are linked to overeating and obesity risk. These might include traits, which reflect high approach tendencies towards food (such as opportunistic

eating, heightened sensitivity to food as a reward) and low avoidance tendencies (such as impaired satiety, weak short term energy compensation) or an interaction between the two (such as excessive snacking of high energy-dense foods, consuming large portions of highly palatable items). For example, a recent cross-sectional observational study by Llewellyn et al. [10] of a population-based cohort of 2258 twins (Twins Early Development Study) tested if satiety responsiveness may serve as an intermediate behavioral phenotype associated with a genetic predisposition to obesity in children. The results of the study showed that associations between the polygenic risk score, which was comprised of 28 common obesity-related single nucleotide polymorphisms (SNPs), and child adiposity were significantly mediated by satiety responsiveness. Thus, the genetic influence on overconsumption might operate through different routes – increasing salience of food, reduced responsiveness to satiation and satiety or a combination of these. The heritable component of BMI could then be expressed through specific eating traits conferred by parents to their children.

Given that BMI is highly heritable with heritability estimates ranging between 70 – 80% for children and adolescents [11], what is the basis of the resemblance? Family and twin studies investigating eating phenotypes among nuclear family members have provided evidence that many dietary and eating behaviors are shared and heritable. For example, an analysis of dietary data collected from adult twins over a 7-day period provided heritability estimates of 42% for daily energy intake, 28% for meal size, and 34% for meal frequency, respectively [12]. Genetic influences have also been observed for meal energy intake in children. In a study by Faith and colleagues [13], 36 monozygotic (MZ) and 18 dizygotic (DZ) twins were invited to the laboratory to consume lunch ad libitum from a multi-item buffet. Children could freely select both the types and amounts of foods and beverages, which showed a range in energy density

(ED; kcal/g). The results of the study indicated that MZ twin pairs were more similar in their meal energy intake (r = 0.80) than DZ twin pairs (r = 0.68) with genetic variations accounting for 24 – 33% of the variance in age- and sex-adjusted total energy intake at the meal.

The control of human appetite is expressed as a complex interaction between psychological, physiologic and metabolic factors involving nutrients in the blood and a host of peripheral hormones, and metabolic and neurotransmitter interactions in the brain. The overlapping sensory, cognitive, hormonal, and metabolic signals that are triggered by the ingestion of food and beverages have been conceptualized within the 'satiety cascade' [14, 15]. This cascade identifies the concepts of satiation, defined as processes that bring an eating episode to an end (intra-meal satiety), and satiety, defined as processes that inhibit further eating in the postprandial period until the next meal (inter-meal satiety). Both satiation and satiety are influenced by physiological signals, which arise from a complex network of hormones and neuropeptides controlling the size of an eating episode (amount consumed) and the interval until the next meal (post-prandial suppression of appetite). Genes which encode these complex appetite and satiety signals are involved therefore in the susceptibility to overeat and in the extent to which external factors such as portion size influence amount eaten.

Specific single gene variants associated with obesity have been identified using genome-wide association study (GWAS) techniques. However, single gene mutations linked to obesity are rare and account for less than 5% of severe obesity [16]. Nevertheless when these are observed they are generally associated with disruption in appetitive pathways and extreme hyperphagia [17]. Disruption to the leptin-melanocortin pathway produces dramatic effects on food intake and body weight. Specifically, congenital deficiency in the leptin receptor is characterized by early onset, severe obesity, and hyperphagia [18].

More common than single gene mutations are SNPs in candidate genes. To date more than 127 SNPs in candidate genes have been identified which can lead to impaired functionality in the central and peripheral regulation of energy balance and have been associated with the human obesity phenotype [19, 20]. **Table 2** depicts examples of some SNPs that have been shown to affect food intake. These include, but are not limited to, polymorphisms in the agouti-related protein (AGRP), fat mass and obesity associated gene (FTO), cholecystokinin (CCK), leptin, monamine oxidase A (MAOA), catechol-o-methyltransferase (COMT), hydroxytryptamine receptor 2A (HTR2A), and peroxisome proliferator-activated receptor gamma (PPARG), which have been shown to be implicated in behavioral traits such as hyperphagia, satiety responsiveness, meal size, snacking behavior, food reinforcement, and macronutrient intake [21-29].

Following a meal, the key peptide signaling satiety is CCK, secreted by the intestine. The CCK1 receptor plays a role in regulating food intake, and CCK generally acts to suppress further food intake. However, in animals who are naturally CCK-1 receptor deficient adult onset diabetes and obesity are observed [30]. Functionality then is compromised when the receptor is absent or impaired. In humans, variations in the H3 haplotype of CCK are linked to extreme portion size consumption [17]. De Krom and colleagues [22] employed an "extreme discordant phenotype" approach by identifying obese adults from the large scale population based European Prospective Study into Cancer and Nutrition (EPIC) cohort who were ranked at the top 5^{th} percentile for self-reported extreme snacking behavior and portion sizes. The results of the study showed significant associations between four of the five CCK SNPs and increased meal size but not snacking frequency, thus carriers of these specific polymorphisms are at risk of consuming large portion sizes, inferring a link to impaired satiety signaling. Interestingly, two of the four

leptin SNPs and one of the eight leptin receptor SNPs were associated with frequent snacking but not with meal size. Therefore, demonstrating two different pathways to extreme eating traits, only one of which relates to the tendency to eat large portions.

Other eating traits have been identified which have been shown to be in part under genetic control and which link to the tendency to overeat. For example, heritability has been established for eating in the absence of hunger (EAH; susceptibility to eating when satiated in response to the presence of palatable snacks; h = 51%) [31], eating rate (h = 62-84%) [32, 33], satiety responsiveness (degree to which an individual ceases eating or chooses not to start eating based on their perceived fullness; h = 65%) [34], and food cue responsiveness (tendency to eat in response to food cues; h = 75%) [34]. While no study to date has established heritability estimates for children's response to portion size, data from the above mentioned studies can be used as a proxy for genetic influences underlying susceptibility to overeat in childhood.

A recent study conducted in weight-discordant siblings provided evidence for significant family correlations for caloric compensation and EAH in children [35]. Caloric compensation, expressed as percentage compensation index (%COMPX), refers to adjustments in intake in response to changes in the ED of a compulsory preload. In this study, 47 same-sex sibling pairs (55% full siblings), ages 5 – 12 years, were invited to consume dinner in the laboratory once a week for three weeks. Twenty minutes before an ad libitum dinner meal, children were asked to consume in full or not to consume one of two pudding preloads which varied in ED (0.57 kcal/g or 0.97 kcal/g). On the day when no preload was served, children were given access to a variety of snacks after they completed the dinner meal. %COMPX was computed as the difference in energy intake at dinner in the two preload conditions divided by the difference in energy intake from the compulsory preloads multiplied by 100. EAH referred to the energy consumed from the

snacks while satiated. The results of the study showed that overweight and obese siblings showed poor caloric compensation and significantly more EAH when compared to their normal-weight siblings. Further, the data showed familial associations for %COMPX and EAH that were significant for full siblings (%COMPX: ICC = 0.36; EAH: ICC = 0.37, $P < 0.05$) but not for half siblings (%COMPX: ICC = 0.02; EAH: ICC = 0.16, $P > 0.05$), which suggests that genetic influences underlie both of these eating traits.

Data by Cecil and colleagues [21] provide further evidence for genetic factors influencing children's compensation ability. In a study with 84 children, ages 4 – 10 years, from 47 schools in Scotland, children were asked to consume in full either a no-energy, low-energy, or high-energy preload, consisting of an orange drink (or water) and a muffin (or no muffin), midmorning on three occasions followed by an ad libitum lunch 90 minutes later. They examined if variants in the nuclear fatty acid receptor peroxisome proliferator-activated receptor gamma (PPARγ) gene (Pro12Ala, C1431T, C-681GI) and the beta-adrenergic receptor (ADRB3) gene (Trp64Arg) were associated with %COMPX. The results of the study showed indeed that children's genotype was a significant factor in children's ability to compensate. Children with polymorphisms in the PPARγ gene (T1431 allele) showed poor compensation whereas children with polymorphisms in the ADRB3 gene (Trp64Arg allele) showed good compensation. When the same cohort of children were enriched for the A allele of the FTO gene, it was found that carriers of this allele were heavier, had a higher fat mass, consumed more energy (even adjusting for their larger body size) and selected more energy as fat in a self-selection test meal, but did not differ in %COMPX. Thus, in this group the FTO risk allele was associated with increased intake, which could be related to opportunistic eating or to a preference for energy-dense, palatable foods.

A study by Wardle and colleagues [23] aimed to test the hypothesis that higher risk FTO alleles would be associated with greater EAH. In this study, 131 4-year-old children from the Twin Early Development Study (TEDS) were given access to three different varieties of biscuits in their homes one hour after children finished eating a meal. Further, children's FTO single nucleotide polymorphism (rs9939609) was determined. The results of the study showed that biscuit intake differed significantly across the three genotype groups (TT, AT, AA). Children with higher risk FTO alleles (AA) showed 25% greater snack intake compared to children with the more protective genotype (TT); an effect which was independent of children's BMI z-score.

In a highly innovative series of studies combining mechanistic analyses of the function of FTO in mice with fMRI scans of human carriers of the AA risk allele, Karra and colleagues [36] found that FTO has a specific regulatory effect on the orexigenic hormone ghrelin. Normal-weight participants with the AA genotype showed a blunted postprandial hunger and ghrelin response to a standard meal and they responded differently to the presentation of food images in the scanner, in both homeostatic (hypothalamus) and reward-relevant brain regions whether satiated or fasted. They also responded differently to the administration of ghrelin, suggesting a perturbation in ghrelin signaling, which is a putative mechanism for observed differences in eating behaviour. The authors suggest that the FTO rs9939609 AA genotype is characterized by an eating phenotype, which could link to obesity risk since these observations were made in normal-weight participants. Clearly this is relevant to identifying characteristics of the pre-obese phenotype in children since enhanced food responsiveness, preferences for high-fat foods, increased appetite and food cue-potentiated eating, part of the FTO phenotype [36], could be identified in children.

Together, these examples illustrate both the eating traits that might be associated with the tendency to respond to portion size manipulations as well as possible mechanisms by which genetic influences shape the underlying phenotype. It is proposed that genes encoding gut hormones and neuropeptides act in concert to control appetite and eating determining meal size and in particular children's response to portion size. While a genetic predisposition may increase some children's susceptibility to overeating when served large portions of foods and beverages, evidence suggests that children's responsiveness to portion size can also be learned behavior. Therefore, biology is not destiny with respect to how much children choose to eat.

Environmental Influences Shaping Eating Traits (Nurture)

The early home food environment plays an important role in shaping children's food preferences and eating behaviors [37-39]. Parents and caregivers influence their children's food choices and eating in a variety of ways. For example, parents serve as important role models for eating [40, 41]. A number of studies have shown significant mother-child relationships in dietary intake including significant positive correlations between maternal and child consumption of sweets and daily energy intake [42] as well as fruits and vegetables [42, 43]. The observed mother-child associations in dietary intake may in part be explained by mothers providing a model of food choices and dietary intake, as well as a marker of shared environmental factors, such as access to the same foods in the same home. Further, the specific feeding strategies and practices parents use have been shown to significantly impact their children's food intake and weight regulation [44]. Parents also decide on the types and quantities of foods and beverages that are being brought into the home and the manner in which meals are being consumed (e.g.,

family meals, self-serve). Additionally, parents influence the physical home environment by selecting dishware (e.g., plates, utensils, cups) sizes and styles and by setting the social norm for appropriate serving sizes. Besides shaping the home food environment, parents make decisions about where to shop for groceries (e.g., grocery stores, wholesale clubs), what promotional tools to use (e.g., grocery coupons), and which restaurant to frequent (e.g., quick serve restaurants that offer value pricing). All of these combine to form the important early home environment.

Data from a recent observational study by Johnson and colleagues [45] in parents and their preschoolers who were recruited from Head Start centers showed that a major driver of how much food children consumed at a meal at home was how much they were served by their parents. In this study, research staff measured amounts served and consumed at a meal by children and parents using digital photography during three home visits. The results of this study showed that amounts served to children by their parents accounted for 73% of the variance in children's intake and children who were served more food showed significantly greater intakes ($r = 0.88$). Interestingly, amounts served to children was significantly correlated with the amounts parents served themselves ($r = 0.51$). These data not only highlight the important role that parents play in establishing portion norms early in children's lives, but they also suggest that parents who consistently serve large portions at home meals may be imparting an expectation that their children will learn to consume them. In a setting where children are expected to "clean the plate" and to avoid waste, especially where families are low income and disadvantaged, setting high social norms for how much is eaten may set in train a pattern of overeating relative to energy requirements.

Besides portions served at home meals, parents influence children's decisions surrounding portion size selection by the feeding styles and practices they use on a day-to-day

basis. One of the aims of a controlled laboratory experiment by Fisher and colleagues [46] was to identify child and family predictors of individual differences in children's self-served portions. In this crossover study, 4- to 6-year-old children were asked to serve themselves macaroni and cheese from a serving dish that contained different portions (275 vs. 550g) of the pasta meal. Parents were asked to complete the Caregiver Feeding Style Questionnaire [47] which assessed the extent to which they used the following four feeding styles: 1) authoritative feeding style, which is characterized by parental involvement, nurturance, reasoning, and structure; 2) authoritarian feeding style, which is characterized by restrictive, punitive, rejecting, and power-assertive parental behaviors; 3) indulgent feeding style, which is characterized by warmth and acceptance in conjunction with a lack of parental monitoring of child's behavior; and 4) uninvolved feeding style, which is characterized by parents showing little control or involvement with the child. The results of this study showed that children of parents who used indulgent and authoritarian feeding styles served themselves about twice as much of the pasta meal and also consumed significantly more calories during the meal than children of parents who used authoritative and uninvolved feeding styles. These data provide evidence for a link between specific parenting styles, feeding practices and consumption of larger food portions even when the child is not under direct supervision of parents.

Parents and caregivers influence child eating via structuring of family meals, modeling eating behaviors, and use of certain feeding practices. They also are in charge of creating the physical home environment. Aspects of the physical home environment that relate to family meals and eating, such as dishware size, can also significantly impact children's selection of food portions. For example, the aim of a recent study by DiSantis and colleagues [48] was to test the effects of dishware size (including plates and bowls) on self-selected portion sizes and intake in a

group of 42 elementary school-aged children who were observed on repeated occasions during school lunch. Children were instructed to serve themselves from three serving bowls at a buffet table containing a main dish, a vegetable side dish, and fruit using either child- or adult-size dishware. The adult-size dishware represented a 100% increase in surface area/volume compared to the child-size dishware. This study showed that children served themselves 90 calories more at lunch when using the adult-size dishware. Further, for every additional calorie that children served themselves, they added 0.43 more calories to their total meal energy intake. Interestingly, the results of this study also showed that food insecurity was a significant predictor of children's response to dishware size in that children from food insecure households self-served significantly more compared to children from food secure households. By way of explanation the authors suggested that larger dishware may have inflated children's norms for consumption and/or may have also altered their visual perception of portion sizes.

In summary, these data illustrate the importance of early influences in children's upbringing and home food environment, which together can help shape children's response to portion size. Neither genetic nor environmental factors work in isolation, however, and it therefore is important to study the interactions between these influences.

Gene-Environment Interactions Underlying Behavioural Susceptibility to Portion Size Response

As discussed in this review, any behavioral tendency to overeat when large portions are available is likely to occur by way of gene-environment interactions. Thus, a genetic predisposition interacts with behavioural and physical aspects of the child's early environment to

facilitate expression of the underlying genotype. In families carrying risk alleles predicting overweight and obesity, genetic effects may be moderated by healthy lifestyle, authoritative parenting, moderate portion sizes, and physical activity. For example, the effects of the FTO risk allele can be attenuated in children by offering healthy diets characterized by lower dietary energy density [49] and in adults by physical activity [50].

Figure 1 provides a conceptual model that illustrates the genetic and environmental influences that can help shape individual eating traits in children. These include genetic factors such as polymorphisms in a multitude of candidate genes that regulate hunger and fullness during and after a meal as well as evidence for select eating behaviors to be heritable. Together, these factors can confer a genetic susceptibility for impaired satiation and/or hyperphagic eating traits in children. Factors in children's early home environment, which include, but are not limited to, parenting styles, feeding practices, family meals, and grocery shopping experiences can also help shape children's eating traits.

The relationship between individual eating traits and the early home environment is likely to be bidirectional in that individual eating traits in children can also influence the type of feeding practices parents use or what stores they frequent to shop for groceries, for example. The greater structural and built environment, which includes the physical home and school environment, children's exposure to advertising, neighborhood characteristics, and the type of restaurants they frequent with their families, can also help shape child eating traits or perceptions of portion size. At the same time, children with a genetic susceptibility to heightened food responsiveness may be actively seeking out environments that offer large portions of palatable foods. Children's response to portion size and accompanied energy intake at meals in turn will in

part be determined by eating traits (e.g., experience of satiety / satiation, responsiveness to visual cues), which have been shaped by children's biological endowment and early home environment.

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482

Table 1: Examples of pediatric studies showing inconsistencies in portion size effects

Child Characteristics / Type of Portion Size Modification	Observed Portion Size Effects?	References
Age (toddler vs. older)	Yes and No	[51, 52]
Weight status (normal-weight vs. overweight/obese)	Yes, No, Maybe	[53-57]
Serving method (self-serve vs. pre-portioned)	Yes and No	[46, 52, 56]
Health foods (fruits and vegetables)	Yes and No	[53, 58]
Interaction with energy density	Yes and No	[59-61]

Table 2: Examples of common gene polymorphisms affecting food intake

Gene	Intake Trait	Reference
AGRP[1]	Macronutrient intake, hyperphagia	[24]
FTO[2]	Satiety, energy intake, energy density, eating in the absence of hunger	[23, 25, 26]
CCK[3]	Meal size	[22]
Leptin	Extreme snacking behavior, hyperphagia	[22, 27]
MAOA[4], COMPT[5]	High-sugar, high-fat intake, food reinforcement	[28, 29]
HTR2A[6] (rs6314)	Food reinforcement	[29]
PPARG[7]	Caloric compensation	[21]

[1]AGRP = agouti-related protein; [2]FTO = fat mass and obesity associated gene; [3]CCK = cholecystokinin; [4]MAOA = monamine oxidase A; [5]COMPT = catechol-o-methyltransferase; [6]HTR2A = hydroxytryptamine receptor 2A; [7]PPARG = peroxisome proliferator-activated receptor gamma

Figure Legend

Figure 1: Conceptual Model for Child Behavioural Susceptibility to Portion Size Response (Adapted from [62])