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Review

A biopsychosocial model of sex differences in children's eating behaviors

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Abstract: The prevalence of obesity and eating disorders varies by sex, but the extent to which sex influences eating behaviors, especially in childhood, has received less attention. The purpose of this paper is to review the literature on sex differences in eating behavior in children and present new findings supporting the role of sex in child appetitive traits and neural responses to food cues. In children, the literature shows sex differences in basic taste response, food acceptance, eating self-regulation, and appetitive traits. New analyses demonstrate that sex interacts with child weight status to differentially influence appetitive traits and neural responses to food cues. Further, neuroimaging results suggest that obesity in female children is positively related to brain reactivity to higher-energy-dense food cues in regions involved with learning, memory, and object recognition, while the opposite was found in males. In addition to differences in how the brain processes information about food, other factors that may contribute to sex differences include parental feeding practices, societal emphasis on dieting, and peer influences. Future studies are needed to confirm these findings, as they may have implications for the development of effective intervention programs to improve dietary behaviors and prevent obesity.

Keywords: sex differences; eating behavior; food intake; biopsychosocial; children; brain imaging

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Introduction:

Sex and gender are important characteristics that contribute to individual variability in the development of disordered eating and obesity, but the extent to which they impact eating behaviors in children is less clear. It has been suggested that sex differences in eating behavior arise in adolescence because of the physiological changes and sociocultural pressures experienced during this developmental period. Prior to adolescence, sex-based influences on eating behavior have been thought to be minimal. However, there are both biological (e.g., sexual dimorphic patterns of *in utero* neural development, sex chromosome effects) and psychosocial (e.g., parental feeding practices, societal body ideals) factors that may affect the way children eat prior to puberty. Despite these potential influences, this period of development has received little attention in the literature. Because of the sex differences that occur in the prevalence of both disordered eating [1-3] and obesity [4, 5], there is a need to understand the role of sex in the development of behaviors involved with the etiology of these diseases prior to puberty. To call attention to this gap in the literature, this paper will review the extant literature and present new data demonstrating that sex differences in eating behavior arise prior to puberty and have effects on children's appetitive traits and neural responses to food cues.

The National Academy of Sciences has outlined rationale for when sex differences should be studied [6]. Several of their criteria apply to eating and weight disorders and therefore are relevant to the current paper. The first criterion is if there are known sex differences in the prevalence or incidence of a disease. Globally, the prevalence of obesity is higher in females than males across all income groups [4] and eating disorders occur nearly 8 times more frequently in females than males [1-3]. These striking statistics provide support for studying the role of sex in eating behaviors because they are integral to the development of these conditions. Another criterion outlined in this report is if there are known sex differences in disease severity, progression, or outcome. In the case of obesity, there are well-described differences in body composition, with adult males carrying fat around the abdomen and chest (i.e., visceral adipose tissue), which is associated with higher metabolic risk, while pre-menopausal adult females are metabolically protected by accumulating fat in the lower extremities [7, 8]. In addition, males tend to have more fat free mass than females. These differences are present throughout development and become more robust at puberty [9]. Furthermore, symptomology associated with binge eating (i.e., frequency, level of distress) is more severe in females relative to males on average. A final criterion suggested in the report is if sex influences the success or outcome of interventions [6]. In both children [10] and adults [11], males tend to be more responsive to weight loss interventions than females. With the potential promise of personalized medicine for treatment of complex diseases like obesity, understanding how sex influences response to treatment could highlight novel therapies that could specifically be targeted to males or females.

Before reviewing the literature, it is important to note that much of the research in this area has not distinguished between the constructs of “sex” and “gender”. Sex refers to the biological classification of male or female according to chromosomes and reproductive organs. Gender, on the other hand, refers to one’s self-representation, which is influenced by sociological and cultural factors [12]. Often one’s biological sex matches with self-assigned gender, but this is not always the case. The multitude of factors influencing both sex and gender have made the study of individual differences between males and females complicated. Because we are applying a biopsychosocial framework to describing sex-effects on eating behavior, we will include discussion of biological factors more likely to influence sex and social and psychological factors more likely to influence gender. However, as most prior studies do not clarify whether they distinguished between the two constructs when collecting participant data, it is not possible to make clear distinctions about how the terminology is used when referring to these studies. In order to avoid switching between “sex” and “gender” throughout the paper, we will use the term “sex” as a combined term that includes not only biological, but also social and psychological influences.

The goal of this paper is to review the literature and present new analyses supporting differential eating behavior characteristics among male and female children. We will also review potential mechanisms that drive these differences using a biopsychosocial framework to guide the discussion. “Eating behavior” will be used as an umbrella term that encompasses children’s oral sensory responses, food acceptance, food intake patterns, eating self-regulation, appetitive traits, and meal-specific microstructural patterns (e.g., bite rate, eating speed). Additionally, to avoid the inclusion of effects on eating behavior that could be influenced by the physiological and hormonal events related to puberty, to the extent possible, the literature search will focus on children age 11 years and under, although it is recognized that this may not fully eliminate pubertal influences. Due to the paucity of evidence in some sections, however, we have included a few studies that report on an age range beyond 11 years, although we recognize that the results may be driven by pubertal development. Within the age group of children discussed, infants will be defined as < 1 year, toddlers will be defined as age 1-2 years, preschool children will be defined as 3-5 years, and middle childhood will include ages 6-11 years.

1. Evidence of sex differences on eating behavior in children

The first section of the paper will review evidence for sex differences in childhood eating behaviors. Based on our general use of the term “eating behavior,” this section will be divided into studies that have examined sex differences in oral sensory responses to taste and flavor, food acceptance, food intake, eating self-regulation, appetitive traits, and meal-specific microstructure.

1.1. Sex differences in oral taste responses:

Taste is a primary driver of food intake [13], therefore, understanding the role of sex in perception and liking of the basic tastes (i.e., bitter, umami, salt, sweet, sour) may have implications for the development of targeted interventions to improve childhood nutrition. Some studies have found that males and females differ in their response to the basic tastes as early as infancy. For example, human newborn females have shown increased acceptance of sweetened formulas compared to males [14], suggesting that differences in taste-guided behaviors may occur early in development. Despite these observations, other studies in newborns have found no sex differences in response to basic tastes, including sweet [15-17]. Sex differences may arise, however, as children grow older because female children and adolescents tend to have lower thresholds for sucrose than males [18-20]. Heightened taste sensations in females may persist across development as female adults are more likely to be classified as "supertasters" of the bitter thiourea compound 6-*n*-propylthiouracil (PROP). This is potentially due to greater density of fungiform taste papillae in females compared to males [21]. However, sex differences in taste anatomy [22] and ability to taste PROP [23] have not been reported in children. Other studies have found that females (ages 6-18 years) are better at identifying taste qualities than males, although no differences were reported in taste intensity ratings [24]. Males tend to like sweeter concentrations of sucrose and lactose than females [19, 25], possibly because females have demonstrated greater taste sensitivity than males across development. Together, these studies suggest the possibility of innate sex differences in the response to basic taste stimuli that may influence hedonic ratings.

In addition to sex differences in response to the basic tastes, there may also be differences in how taste perception relates to more complex behaviors like food acceptance and intake. For example, female preschool children who were non-tasters of PROP had higher liking of full-fat milk and reported greater parentally reported intake of discretionary fats (i.e., salad dressings, toppings, and spreads) than males [23]. Similarly, while male non-taster children reported greater intake of soy-containing foods than males who were tasters, the relationship was opposite in females [26]. Because there is no difference in taste anatomy (i.e., fungiform papillae) [22] or bitter taste sensitivity reported in children, the observed sex differences in the relationship between PROP status and diet suggest that environmental influences on feeding (e.g., parental feeding practices) might drive these reported sex differences. This will be discussed in more detail in the second part of the paper.

1.2. Sex differences in food acceptance/preference:

The impact of sex on liking and perception of basic tastes suggests there may also be sex differences in food acceptance (i.e., hedonic response measured independently of another food/beverage) or preference (i.e., hedonic ranking of a food/beverage compared to other options) [27, 28]. Cooke and colleagues [29] found that females (ages 4-7 years old) liked a greater number of foods than male children. With regards to specific foods or food groups, studies including children from various countries have consistently shown that females rate liking of fruits [29-32] and vegetables [29-35] higher than males, while male children report higher liking for meat, fish, poultry, and high-fat foods compared to females [29-31, 36]. Furthermore, male children in middle childhood have higher acceptance of fatty and sugary foods [29] and foods and beverages characterized as "unhealthy" (e.g., sweet snacks, savory snacks, sugar sweetened beverages) compared to female children [31]. Additionally, as children grow older, females tend to increase liking for vegetables [33] while males tend to increase liking for meat products [29].

While the aforementioned studies demonstrate sex differences in food acceptance in middle childhood, studies in toddlers and preschool-aged children have shown no differences [37] [38]. However, it is not clear if null findings are in part due to a lack of sensitivity in the methods available to measure liking in preschool children (i.e., hedonic facial scales, parental report). In summary, these results demonstrate that females in middle childhood typically like or prefer foods that are often regarded as lower in energy, but nutrient dense, such as fruits and vegetables, whereas males tend to like meats, meat products, and foods high in fat and sugar. The sensory and/or nutritional characteristics of the foods that drive these sex-effects are not known.

1.3. Sex differences in food intake:

As liking and preference are primary determinants of what children eat [39, 40], it is likely that sex also influences children's dietary intake. This is especially apparent for fruits and vegetables [39]. In children as young as 2 years, intake of vegetables [41-44], fruits [35, 42, 43, 45] and fruits and vegetables combined [42, 46-48] is higher among females than males. Female children have similarly reported greater intake of foods classified as "healthy" and lower intake of "unhealthy" foods when compared to males [43]. Since these studies used self- and parentally-reported measures of food intake, there is potential for response bias as fruit and vegetable intake is a socially desirable behavior. However, studies that have used more objective assessment methods in schools have also observed that female students are more likely to consume from a salad bar than males [49, 50].The alignment with observational data strengthens the findings from questionnaires, suggesting that female children tend to consume more fruits and vegetables than males.

In addition to fruits and vegetables, self-reported intake of other foods and food groups also varies by sex. In cohorts of European children, males report consuming more sugar and sweets [47, 51], breakfast cereals, full-fat milk, meats/meat products, and baked beans while females consumed more oily fish, eggs, and cheese [47]. In the United States, male children tend to have higher intake of most food groups, as well as higher overall energy intake [48, 52], although overall variety of foods consumed tends to be higher in females [53]. This finding supports the previously discussed observations that found females also *liked* a greater number of foods than male children [29]. Although these studies provide support for the notion that sex differences in eating behavior arise in childhood, not all studies agree [38, 54]. Inconsistencies across studies could be due to variability in how dietary intake is measured (e.g., 24-hour recall, food frequency, direct observation), who is reporting dietary intake (e.g., parent vs. child), and the age and cognitive abilities of the child being studied [55]. There is a need to conduct more observational studies where food intake is directly measured to confirm sex-effects on reported intake in children.

1.4. Evidence of sex-effects on eating self-regulation in children:

Self-regulation is a multi-dimensional construct referring to one's ability to manage thoughts, actions, and emotions in favor of reaching a desired goal [56, 57]. Poor self-regulation early in life has been associated with negative health outcomes in adulthood [58], including obesity [59, 60]. Sex differences in self-regulation, assessed by the delay of gratification task, were first reported by Mischel and Underwood [61] who found that female preschool children could wait longer to receive a tasty treat (i.e., a marshmallow) than male children. A more recent meta-analyses that included both children and adults also confirms females show better delay of gratification for food than males [62]. The early emergence of sex differences in self-regulation suggests that observed differences in children's eating behaviors may in part be related to differences in the ability to adhere to dietary goals more broadly.

Related to the broader concept of self-regulation is eating-related self-regulation, or the ability to begin and end an eating event in response to internal cues of hunger and fullness [63]. While the extent to which these two constructs are related has been debated, it has been suggested that eating self-regulation is a domain-specific manifestation of broader self-regulatory capacity [64]. Based on this apparent relationship, we might expect to see better eating self-regulation in female relative to male children. However, in studies that have assessed eating self-regulation using the compensation protocol, this has generally not been the case [67, 68, 70, 71]. Compensation or preloading trials are typically done using a crossover design where children consume appetizers or 'preloads' on two separate visits. These preloads are matched for taste, sensory characteristics, and often volume, but are covertly manipulated to vary in energy density (kcal per weight or volume of food or beverage) and/or macronutrient content. Participants are compelled to finish the preload and are served an *ad libitum* meal some time later (often 25-30 minutes with children) to measure consumption. Children who have "good" energy compensation can adjust their intake at the subsequent meal based on the energy content of the preload [65, 66]. Poorer compensation ability has been associated with higher weight status in children [67-69], suggesting that performance on this measure may generalize to eating regulation more broadly. Several studies that have used this protocol in preschool children found that males have better energy compensation than females [67, 68, 70, 71], which is consistent with studies in adults [72, 73]. Notably, other studies in preschool children do not report sex differences [74, 75] [76] and the individual variability in this measure is poorly understood. Of note, all the studies that have found that males compensate better than females have used beverages as a preload, raising the possibility that sex differences in energy compensation are specific to the ability to regulate calories in liquid rather than solid form.

The notion that sex differences around eating self-regulation are specific to beverages is further supported by studies that have tested the effect of varying the energy density of a beverage served *within* a meal. Whereas the traditional preloading study measures "satiety" by testing the extent to which a preload or snack delays hunger at the following meal, serving a beverage within a meal captures "satiation" by determining the effect of varying energy content on total meal intake. Kling and colleagues [77] tested the effect of varying the energy density (ED) of milk on satiation by conducting a crossover study where either lower- (1% fat) or higher- (3.25% fat) ED milk was served to children with a typical preschool meal served in a childcare setting. When the higher-ED milk was served, males decreased their intake of the other meal items, whereas females did not. Thus, compared to males, females were less accurate at adjusting their intake to account for additional energy consumed from the higher-ED milk. These sex differences were independent of possible confounders, including the type of milk children consumed at home, child age and body size, milk liking and preference ratings, children's appetitive traits, and parent feeding practices. The consistent pattern of sex differences observed in both satiety and satiation studies challenges the notion that compensatory responses are solely due to the delay between the preload and subsequent meal that allows for the release of sensory and nutrient signals that influence fullness. Other possible explanations of these sex differences are differences in the response to food sensory properties [23], social expectations placed on males and females [78], or sex-effects on meal time behaviors [79]. Additionally, subtle differences in children's body composition present prior to puberty [9] could also promote males' advantage at energy compensation as fat free mass is the primary determinant of metabolic rate and, hence, energy needs. However, these speculations require further investigation to confirm.

1.5. Sex differences in child appetitive traits and Eating in the Absence of Hunger:

Several studies have investigated whether there are sex differences among other appetitive traits assessed by the Children's Eating Behavior Questionnaire (CEBQ) [80]. The CEBQ is a 35-item parental report instrument that assesses child appetitive traits which can be grouped into those related to food avoidance (i.e., slowness in eating, satiety responsiveness, emotional undereating, and food fussiness) and those related to food approach (i.e., enjoyment of food, food responsiveness, desire to drink, and emotional overeating) [80]. Higher scores on food approach related subscales and lower scores on food avoidant related subscales have been positively associated with weight status in children [81-83]. Several prior studies have examined whether subscales of the CEBQ vary by sex. A cohort in middle childhood from Thailand found that males had greater enjoyment of food than females [84], however the opposite was found in a cohort of 6- to 7-year-old Dutch children (i.e., females higher than males) [85]. When looking more broadly across appetitive traits, male children showed greater desire to drink [84], emotional overeating [85], and food responsiveness [86]. In contrast, females showed greater avoidance behaviors (e.g., slowness of eating, satiety responsiveness) [87] [81].

In order to better understand whether appetitive traits differ by sex, age, and adiposity, we examined CEBQ scores from 11 data sets collected from studies conducted at the Children's Eating Behavior Laboratory at The Pennsylvania State University from 2012 – 2018. A total of 263 (M=133; 50.6%) 3- to 12-year-old children had complete parent-reported anthropomorphic and CEBQ data as well as measured child anthropometrics. Males and females did not differ by age ($t(260)=0.553$, $P=0.581$, $d=0.07$), body mass index (BMI)-for-age percentile (BMI%; $t(260)=-0.859$, $P=0.391$; $d=0.11$), race (Fisher's $P=0.276$), ethnicity (Fisher's $P=0.999$), maternal education ($t(260)=0.551$, $P=0.58$, $d=0.07$;), or CEBQ subscales (P values ranging from 0.073 – 0.681; see Supplementary Materials (SM) Table S1). Although maternal education did not differ by child sex, it was used as a proxy for socioeconomic status as maternal education has been shown to be more highly associated with adiposity than income [88]. Child weight status was assessed by measuring height and weight on a digital scale (Tanita, Arlington Heights, IL) and stadiometer (SECA, Chino, CA) and children were categorized as either having healthy weight (BMI-for-age < 85th percentile) or overweight/obesity (BMI-for-age ≥ 85th percentile). [Table 1]

Table 1. Demographic Characteristics.

	CEBQ		fMRI	
	Males (n=133)	Females (n=130)	Males (n=20)	Females (n=25)
Age (yrs)	7.40 (2.28)	7.56 (2.10)	8.75(0.99)	9.06(1.34)
BMI percentile	61.53 (29.06)	58.50 (28.20)	52.50(27.12)	53.57(30.93)
Maternal Ed. (yrs)	16.19 (2.63)	16.35 (2.71)	16.91(2.49)	16.88(1.90)
Weight Status (n)				
Obese/Overweight	43	27	3	6
Healthy Weight	90	103	19	19
Ethnicity (n)				
Not Hispanic/Latinx	94	84	20	25
Hispanic/Latinx	4	4	1	0
Not Reported	35	35	1	0
Race (n)				
Black/African American	6	2	2	0
White	119	112	19	25
Other	7	4	1	0
Not Reported	1	2	0	0
SES (n)				
> $100,000	16	19	7	5
$51,000-$100,000	30	29	11	15
<= $50,000	18	18	3	5
Not Reported	69	64	1	0

Means (SD) reported for Age, BMI percentile, and Maternal Education. Weight Status categories defined by BMI percentile: Obese/Overweight ≥ 85th percentile; Healthy Weight < 85th percentile. BMI: body-mass index; CEBQ: Child Eating Behaviors Questionnaire Sample; fMRI: functional Magnetic Resonance Imaging Sample.

Food approach and avoidance, as measured with CEBQ, were examined separately using the same hierarchical model steps—1: child age and maternal education; 2: a quadratic age term; 3: child sex and adiposity; 4: a sex X age interaction; and 5: a sex X adiposity interaction (Table 2). The change in model fit, R^2, was tested at each step to determine whether the model explained significantly more variance with the added terms. Once the best model was identified, exploratory analyses examined the component subscales that contribute to the food avoidance and approach scores to determine whether the effect seen was consistent across subscales or driven by an individual subscale.

Individual differences in CEBQ avoidance and approach behaviors were best fit by different models. Child sex was not a significant predictor of avoidance for any of the models where it was included. In contrast, food approach was best modeled by including the interaction between child sex and weight status (Table 2). The interaction between sex and weight status was significant such that the association between having overweight or obesity and greater food approach was stronger for females than males. This suggests that weight status may be more predictive of food approach behaviors in females than in males. Exploratory analyses of approach subscales indicated that this finding was primarily driven by the food responsiveness subscale which showed a suggested sex by weight status interaction (β(SE) = -0.36 (0.20), p = 0.073). The interactions between weight status and other CEBQ approach subscales were not significant (*P* values ranging from 0.155-0.255). Overall, these results suggest that in female children, food responsiveness could be a better predictor of weight status than other CEBQ approach subscales, and therefore may be a target for intervention studies in this population.

Although the ability to reliably assess appetitive traits quickly via parent-report is valuable to the study of eating behaviors in children, it is equally important to identify how laboratory assessments of overconsumption relate to sex in children. Eating in the absence of hunger (EAH) is a standard paradigm to assess hedonic eating [89-91] and has been shown to be stable through childhood [92] and a phenotype for childhood obesity [93]. Studies in preschoolers [74] [93] and middle childhood [94] have found greater eating in the absence of hunger in males compared to females. However, in 5- to 18-year-old Hispanic children from the United States, sex differences did not persist after adjusting for energy needs [95]. Similar to reported findings on food approach, individual differences in eating in the absence of hunger were associated with weight status [69, 94, 96, 97], parental dieting characteristics, and feeding practices [90, 96] in females but not males. Together, these findings suggest that eating in the absence of hunger and food approach traits are associated with individual differences (e.g., weight status, parental feeding practices) in females, but not in males. [Table 2]

Table 2. Hierarchical Regression for Approach and Avoidance Scales of the Child Eating Behavior Questionnaire

	Approach														
	1			2			3			4			5		
	B	SE	β	B	SE	β	B	SE	β	B	SE	β	B	SE	β
Maternal Education	-0.005	0.01	-0.027	-0.005	0.01	-0.028	-0.005	0.01	-0.025	-0.005	0.01	-0.025	-0.003	0.01	-0.015
Age	0.008	0.01	0.034	-0.003	0.09	-0.015	0.0003	0.09	-0.001	0.001	0.02	0.003	-0.002	0.01	-0.008
Age^2				0.001	0.01	0.050	--	--	--	--	--	--	--	--	--
Weight Status							0.288	0.07	**0.572*****	0.288	0.07	**0.571*****	0.455	0.11	**0.902*****
Sex							-0.119	0.06	**-0.237†**	-0.107	0.22	-0.002	-0.046	0.07	-0.091
Sex X Age										-0.002	0.03	-0.007	--	--	--
Sex X Weight Status													-0.286	0.14	**-0.567***
R^2			0.002			0.002			0.071			0.071			0.086
$^A\Delta$ R^2 F-statistic						^{1}0.017			**^{1}9.591*****			^{3}0.003			**^{3}4.212***
	Avoid														
Maternal Education	0.017	0.01	0.094	0.016	0.01	0.093	0.017	0.01	0.094	0.017	0.01	0.097	0.017	0.01	0.093
Age	-0.029	0.01	**-0.137***	-0.072	0.08	-0.339	-0.027	0.01	**-0.126***	-0.035	0.02	-0.165	-0.026	0.01	**-0.125***
Age^2				0.003	0.01	0.205	--	--	--	--	--	--	--	--	**--**
Weight Status							-0.073	0.07	-0.156	-0.071	0.07	**0.151†**	-0.087	0.10	-0.184
Sex							0.068	0.06	0.143	-0.049	0.21	0.143	--	--	--
Sex X Age										0.015	0.03	0.072	0.062	0.07	0.131
Sex X Weight Status													0.023	0.13	0.049
R^2			0.029			0.030			0.038			0.039			0.038
$^A\Delta$ R^2 F-statistic						^{1}0.303			^{1}1.137			^{1}0.871			^{1}0.765

Unstandardized coefficient (B) and standard errors are presented along with the standardized β for steps 1-5.

A: superscript number indicates step model was compared to

† $p<0.10$, *$p<0.05$, **$p<0.01$, ***$p<0.001$

Meal-related microstructure:

Microstructural components of a meal include bite rate, eating rate, and bite size [98]. Of these characteristics, eating rate has been most consistently associated with weight status in adults [99] and children [100], and is therefore a target for interventions to treat obesity [101]. Observational coding of meal-time behaviors in the GUSTO cohort from Singapore showed that male children have faster eating rate (g/min), larger bite size (g/bite), and shorter oral exposure (min) than female children [102]. Similar findings have been reported in adolescents [103, 104]. While the research in this area is limited, the observation of sex differences in eating speed and oral processing time prior to puberty has implications for the development of personalized interventions to reduce overeating in males and females.

While there is a lack of studies that have included sex as a primary determinant of eating behaviors, the reviewed findings are suggestive of male-female differences in basic taste response, food liking and intake, eating self-regulation, appetitive traits, and meal-related microstructure. Since these differences could impact the success of dietary and behavioral interventions [10], additional research focused on investigating sex differences in pre-pubertal children is needed to confirm these finding as well as identify mechanisms driving these early-life differences.

2. Biopsychosocial contributions to sex differences

The second part of the paper will explore possible mechanisms for the observed sex differences in children's eating behaviors. The scope of the discussion has been limited to potential biological influences (i.e., neural responses to food cues), psychological influences (i.e., body image and weight concerns), and social influences (i.e., parental feeding styles and practices). Additional potential influences are presented in Figure 1, but will not be explored at length in this paper.

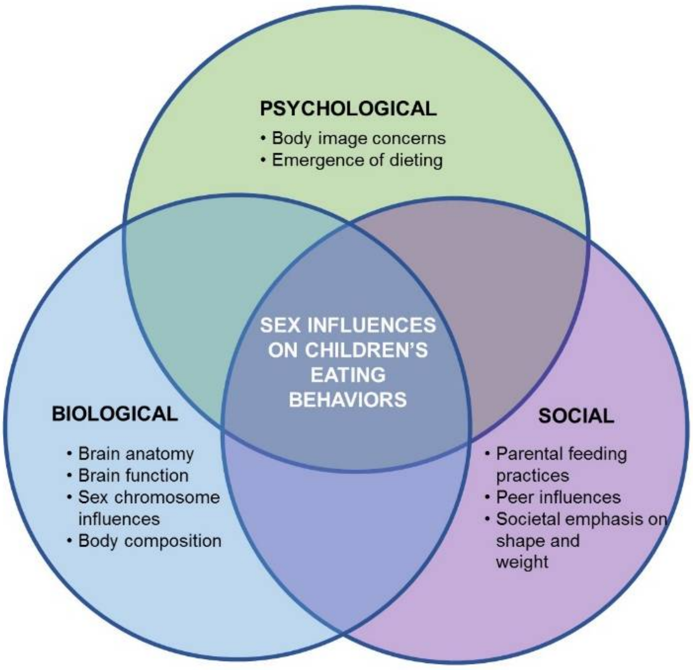

Figure 1. Biopsychosocial model of sex effects on children's eating behaviors. Potential biological influences could come from differences in brain anatomy or brain function that arise early in development, effects due to sex chromosomes, or differences in body composition that can influence food intake regulation. Psychological influences include body image concerns and the emergence of dieting, typically observed more frequently in females than males. Social influences include differences in parental feeding practices directed at males and females, peer influences, and societal pressures emphasis on "thinness" in females and "bigness" in males.

2.1. Neural differences in the response to food cues.

One potential contribution to explain differences in eating behavior between male and female children is variation in neural processing of food cues. Food cues elicit responses in brain regions implicated in executive function, subjective valuation (e.g., orbitofrontal cortex), and visual processing (e.g., fusiform gyrus) [105] that are correlated with eating behaviors [106, 107]. Several studies have observed sex differences in neural response to food cues. For example, in adult samples that have used functional magnetic resonance imaging (fMRI) to asses food cue reactivity, females show greater activation than males in a number of brain regions associated with executive function (i.e., dorsolateral and ventromedial prefrontal cortex)[108, 109], visual processing [110](e.g., fusiform gyrus), taste and interoceptive processing[110](e.g., insula), and reward (e.g., caudate) [111]. To date, only one study has reported sex differences in children, although the findings contradicted those from adults. Luo and colleagues [112] found that compared to females, 7-11 year-old males had greater activation to food relative to non-food images in the right posterior hippocampus and temporal occipital fusiform cortex, regions implicated in memory and visual processing. To date, the developmental trajectory of neural response to food cues remains unclear, making it difficult to interpret the inconsistent patterns of sex differences between adult and child samples.

To further investigate and potentially confirm the findings of Luo and colleagues [112], we conducted a secondary data analysis in a similar age group (age 7-11 years; see demographic characteristics in Table 1) to determine whether male and female children differed in their neural processing of food images that varied in energy density and portion size. Males (N=22) and females (N=25) did not differ by age ($t(45)=0.89$, $P=0.378$, $d=0.260$), BMI-for-age % ($t(45)=0.125$, $P=0.901$, $d=0.036$), race (Fisher's $p=0.095$), ethnicity (Fisher's $p=0.456$), or maternal years of education ($t(45)=-0.045$, $P=0.964$, d=0.013).

On the day of the MRI, children arrived after a 2-hour fast and were scanned during a usual meal-time. Before and after the scan, children rated fullness level on a validated, pictorial visual analogue scale [113]. Children were imaged at 3T (MAGNETOM Trio) with a T1-weighted structural (MPRAGE) sequence and a T2*-sensitive gradient echo pulse sequence (see supplementary materials (SM) for image acquisition parameters). Food images were presented using MATLAB Version 8 [114] and viewed through a mirror mounted on the head coil using a magnet-compatible projector. The protocol for task design and image development has been reported elsewhere [107, 115]. In brief, children viewed a total of 180 images (120 food, 30 furniture, 30 scrambled images) presented in block design. The food cues differed in portion size (large, small) and energy density (high-ED, low-ED). High-ED foods were > 1.5 kcal/gram and included French fries, chicken nuggets, cookies, and pizza. Low-ED foods were < 1.5 kcal/gram and included grilled chicken, carrots, broccoli, and apples. Data were preprocessed and analyzed using Analysis of Functional NeuroImages (AFNI) [116] using standard preprocessing steps (See SM for details). Four participants (3 Male, 1 Female) were excluded due to excessive motion (defined as fewer than 4/6 usable runs; see SM for motion and outlier criteria). For each subject, a general linear model was constructed including 6 parameters of interest (i.e., one for each image condition) and 12 parameters of no-interest to control for motion (see SM). Group analyses were then conducted using energy density contrasts (high-ED - low-ED) derived from parameter estimates for each portion size condition separately, as well as a composite (i.e., across both portion sizes). Multiple comparisons were controlled by using Monte-Carlo simulations ([117] $P < 0.001$; $k=29$) using AFNI's 3dClustSim to achieve a final $P< 0.05$.

As there was no main effect of portion size, or a portion size X sex interaction on neural response to high- or low-ED cues (see SM), the remaining group analyses focused on the ED contrast collapsed across portion size. An analysis of covariance (ANCOVA; 3dMVM,[118]) showed a significant sex X BMI z-score interaction in right superior temporal gyrus, extending to both parahippocampal and fusiform gyri F(1,39)=29.21; peak: x=-37.5, y=37.5, z=7.5; k-173; Figure 2A). Post-hoc correlations confirmed a significant positive association between BMI z-score and BOLD response to higher (compared to lower) ED food images in females ($R=0.598$; $P =0.002$), while in males this relationship was negative ($R=-0.667$; $P =0.002$) [Figure 2B]. There was no evidence for a main effect of BMI z-score or sex. Although pre- and post-scan fullness differed in males and females, the same pattern of results was seen when controlling for fullness ratings and when analyses included ED contrasts for each portion size (see SM). [Figures 2A, 2B]

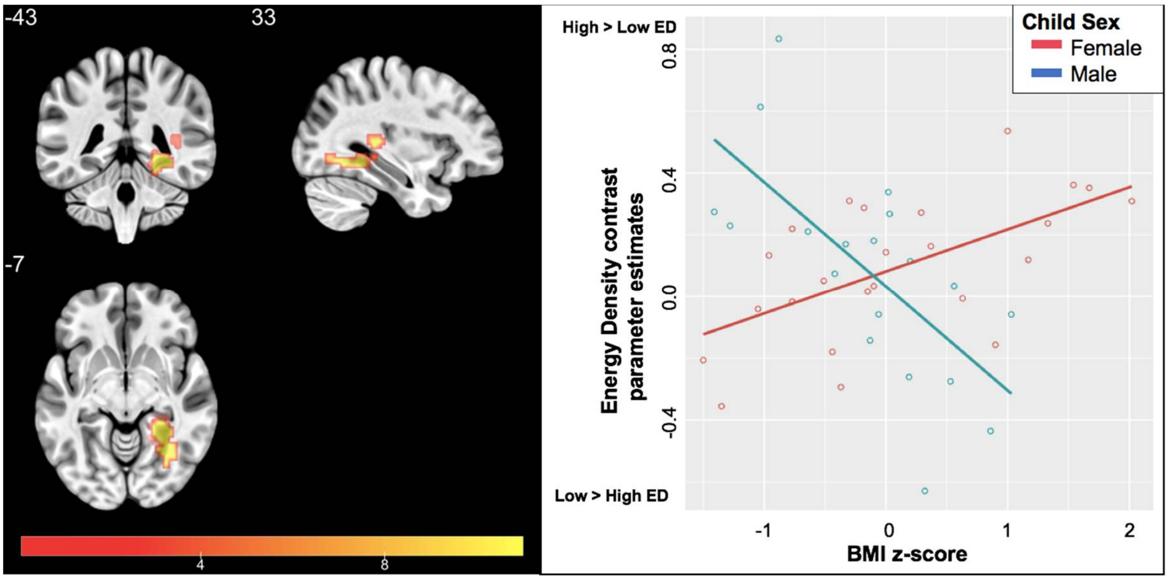

Figure 2. Left: Statistical parametric map (F-statistic) of the interaction between BMIz and child sex on neural responses to high-ED compared to Low-ED food cues. Cluster extends from the right superior temporal gyrus into the parahippocampal and fusiform gyri. Right: Extracted energy density contrast (high-ED – low-ED) parameter estimates, illustrating increased activation to high-ED compared to low-ED food cues for girls with BMIz greater than the 50th percentile and increased activation to high-ED compared to low-ED food cues for boys with BMIz greater below the 50th percentile.

Although preliminary, these results suggest that increased weight status in female children is positively related to brain activation to higher-ED food cues in regions typically associated with learning, memory (i.e., parahippocampal gyrus) and visual object recognition (i.e., fusiform gyrus), while in male children the opposite pattern was observed. Future studies are needed to confirm these findings and determine their long-term implications.

2.2. Body image and weight concerns.

From a young age, individual differences in eating behaviors may be, in part, driven by sex differences in perceived ideal and preferred body size. Sex differences in dieting and body image concerns have been consistently documented in children as young as 8 years [119]; however, differences in younger children are less consistent [119-121]. Compared to males, school-aged females report higher levels of weight-related behaviors and concerns, including desire to lose weight [122], dieting behavior [120], level of worry about weight [120, 123-125], thoughts about which foods might promote weight gain [120, 123, 125], and feelings of guilt over eating too much [123]. Females also tend to be more dissatisfied with their bodies [121, 122, 124, 126, 127] and have lower self-esteems [127-129]. By 8 years of age, females have greater body dissatisfaction than males [119, 121-124, 129, 130] and this tends to increase during middle childhood [129]. Overall, greater emphasis on the maintenance of an ideal body weight in females than males may encourage sex differences in eating behaviors that are adopted to achieve “the perfect figure”.

2.3. Parental feeding styles and practices.

The greater emphasis on “thinness” as a cultural ideal in females likely encourages sex differences in parental feeding practices and attitudes directed at children. In general, parents are more concerned about weight status in female children than they are in males [122, 131]; thus, they are more likely to assume an active role in training, redirecting, and encouraging healthful eating behaviors in female children [122, 131]. Several studies have also found that male children are encouraged to eat more than female children [132, 133], while females are more likely to seek parental praise and approval for meal-time behaviors [132]. In response to maternal concerns, female children are more likely than male children to change eating behaviors [130, 134]. These observations could help to partially explain sex differences in food acceptance and intake, whereby female children show more nutritious food intake patterns than males [43]. Greater need for external attentions, like praise, among females could mean that they are less attentive to internal signals of hunger and fullness when compared to males, which may increase their risk for disordered eating behaviors.

The influence of controlling feeding practices, like restriction and pressure-to-eat, have also been found to vary depending on the sex of the child. Greater laboratory [90, 135] and parentally-reported restriction [68, 136, 137] have been associated with higher weight status in primarily Caucasian females, but not males. In addition, Arredondo and colleagues [138] have found in Latino families that greater parental control over feeding is associated with increased reported intake of "unhealthy" foods (e.g., sodas, sugar sweetened beverages, chips, sweetened cereals) in females, but not males. In general, mothers tend to use greater feeding control with female than male children[139]. Increased use of parental control, specifically within the domain of feeding, may weaken females' ability to eat in response to internal satiety signals, which may ultimately increase weight gain and risk for obesity. Notably, these patterns have not been consistently observed across studies. Studies in both preschool children [140] and a Dutch sample in middle childhood [141] found that controlling feeding practices were associated with greater eating in the absence of hunger [140] and external and emotional eating [141] in males, but not females. Overall, the influence of child age, ethnicity, and socioeconomic status, as well as parental factors including education, weight status, and general parenting style have not been clarified and require additional investigation.

2.4. Peer and social influences.

In addition to parental influences that may serve to engender children with different eating behaviors, societal ideals include expectations about what and how males and females should eat. A feminine identify is characterized by eating smaller portions, consuming less meat, and preferring healthier options to maintain appearance, while a masculine eating identify is characterized by feeling full, with a focus on physical performance [142, 143]. Within these ideals, female children are seen as a more effective at modeling healthy behaviors than males [144, 145]. Furthermore, females are also more likely to respond to modeled eating behaviors including vegetable acceptance [144] and fruit and vegetable intake[146]. The higher success of modeling and dietary interventions among females suggests a greater awareness of social expectations related to eating [147]. Moreover, greater self-control among females [59, 78] may help facilitate greater uptake of these behaviors.

3. Conclusions and recommendations for future research

In this paper, we reviewed evidence of sex differences in children's eating behaviors and presented new data showing that sex and weight status interact to differentially influence appetitive traits and neural response to food images in males and females. In the reviewed literature, we identified differences in basic taste response and acuity, food acceptance, food intake, appetitive traits, and eating rate between male and female children. In addition, new analyses showed that child weight status interacts with sex to influence appetitive traits such that food approach behaviors (i.e., food responsiveness) are stronger predictors of increased weight status in females than in males. Similarly, in a separate cohort of 7- to 11-year-olds, we found that sex and weight status interact to influence children's neural responses to food images that vary in energy density. In females, greater activation to higher energy food cues in brain regions implicated in learning, memory, and object recognition was positively related to weight status, while the opposite pattern was observed in males. Although we cannot fully discount the possibility that some of the observed differences are driven by physiological changes that occur with puberty, the focus on children under 11 years of age likely reduces these influences. The evidence presented underscores the need to study the etiology and implications of sex differences in children's eating behaviors.

Despite inconsistencies across the literature, a few consistent themes are apparent. First, sex differences in children's eating behaviors were more often found in school-aged children. Few consistent differences in eating behaviors were identified among infants and toddlers. It is possible that differences are present in younger children, but unable to be measured due to methodological limitations. Perhaps more likely, however, is that these patterns arise during childhood due to differential parenting practices and social influences directed at males and females. Second, female children tend to report liking and eating more foods that are lower in energy density and higher in critical nutrients (i.e., fruits and vegetables) than males. Due to the lack of clear biological differences in taste anatomy, these differences are also likely to be influenced by parent, peer, and societal factors. Importantly, the self-report nature of most of this literature highlights the need to confirm these findings with more objective measures of eating behavior. Third, sex differences in appetitive traits, EAH, and parental feeding attitudes are influenced by complex interactions with child weight status. In general, parents are more concerned about excess weight in female compared to male children. As a result, they likely feed children differently depending not only on the sex of the child, but also their perception that the child is at risk for developing overweight. It is likely that parental characteristics, like dieting history, cognitive restraint, socioeconomic status, and weight status influence the relationship between child sex and eating behaviors, highlighting the need to conduct larger studies that are sufficiently powered to query three-way interactions (e.g., child sex X child weight status X parent weight history).

Caution is recommended when interpreting the findings discussed, both from the literature and the new analyses presented. First, the majority of studies that have reported sex differences were not designed to detect sex as a primary determinant of outcomes; thus, it is not possible to rule out chance findings. Second, among the studies that did not report differences, sex was often controlled for as a covariate, but results for main outcomes were not stratified and reported by sex. This makes it difficult to determine whether primary eating behavior outcomes differed in males and females and limits the ability to conduct meta-analyses across studies. Third, determining the underlying mechanisms for sex differences in eating behavior is complicated by the lack of clarity in how sex and gender are defined in the literature. A concern moving forward is that researchers will overgeneralize findings by developing separate intervention approaches for males and females without considering that sex and gender are non-binary, multidimensional constructs. To avoid this type of overgeneralization, we caution against using sex or gender as the basis to group participants prior to assigning treatments. Instead, sex and gender should be measured and considered like other individual subject characteristics, and used to provide information to help phenotype risk groups.

When planning and reporting on future studies, it is important that researchers clearly define the constructs of sex and gender, in terms of how they are measured and reported. In addition, in studies that statistically control for sex as a covariate, it would be helpful for researchers to report applicable estimates, coefficients, and p-values for covariates, either in the manuscript or in supplementary data. This would facilitate the ability to conduct systematic reviews on this topic. Moreover, research in children, especially infants and preschool children, should utilize objective and observational measures of children's eating behaviors and intake when possible to limit the influence of parental beliefs and perceptions along with probable response bias for questionnaires. Lastly, in regards to intervention efforts for obesity, sex or gender should be considered when determining target behaviors as well as evaluating the impact of the intervention on primary and secondary outcomes. Together, these recommendations will help advance our understanding of the role that sex and gender play in the development of weight and eating disorders.

In conclusion, children exhibit sex differences in basic taste response and acuity, food acceptance, food intake, appetitive traits, and eating rate that are unlikely to be driven solely by puberty. In addition, new analyses show that child weight status interacts with sex to influence appetitive traits and the neural response to food cues. Generally, female children are more responsive to socially driven expectations about how and what they should eat, while male children may be less attentive to these cues. The reported differences between males and females have implications for intervention. Females' inclination to more readily adopt modelled eating behaviors could diminish responsiveness to internal cues of hunger and fullness, but may result in greater adherence to dietary goals and interventions. On the other hand, males may be less at risk for overriding internal cues, but may not respond as readily to typical intervention techniques. These potential implications underscore the importance of understanding the mechanisms underlying sex differences in order to prevent development of maladaptive eating behaviors.

Supplementary materials: Additional details and results from the fMRI scanning paradigm and analyses are included in the supplementary materials.

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